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THE BONE LESIONS OF SMALLPOX [1]

SECOND REPORT

By W. E. MUSGRAVE and A. G. SISON

PATHOLOGICAL REPORT

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Eleven plates and 5 skiagrams

Since the publication of our preliminary article on the bone lesions of smallpox,[2] we have had the opportunity to study several other cases of which 12 are briefly reported here. Skiagrams were taken of the affected bones and joints; and in one case post-mortem examination was made by Dr. B. C. Crowell [3] and the findings are included as a part of this report.

DISTRIBUTION OF THE LESIONS

In the preliminary report we stated that "One of the most striking features of the deformities is the constant location of the lesions in the upper extremities." Further study has shown this statement to be an error.

Any of the bones and joints of the body may be affected. However, the long bones and their articulations are more fre-

[1] Read before the Ninth Annual Meeting of the Philippine Islands Medical Association, held in Manila from November 4–7, 1912.

[2] *This Journal, Sec. B* (1910), 5, 553.

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quently affected than are other bones and joints. In the order of frequency, the following locations of the lesions may be noted:

(1) The bones and joints of the upper extremity.
(2) The bones and joints of the lower extremity.
(3) The bones and joints of the other parts of the body.

The bones of the upper extremity may be involved in the following order of frequency:

(*a*) Forearm (radius and ulna).
(*b*) Arm (humerus).
(*c*) Hand (carpal, metacarpal, and phalanges—proximal and distal).

The bones of the lower extremity may be also involved in the following order:

(*a*) Leg (tibia and fibula).
(*b*) Thigh (femur).
(*c*) Foot (tarsal, metatarsal, and phalanges—proximal and distal).

In regard to age, the bone lesions usually are observed in persons with a history of having had smallpox during early childhood, but the deformity may follow variola contracted at any time before the complete ossification of the bones. The oldest age in which such a complication of variola has been observed occurred in a boy 14 years old.

DISCUSSION

The fact that practically no mention of bone-deforming lesions as a complication of variola is found in current literature should make one very cautious not to interpret coincidence as cause and effect. The fact that the masses of the Filipino people are undernourished and underdeveloped as a result of starvation and metabolism incongruities adds to the difficulty of definite conclusions in interpreting the etiology of chronic bone-deforming lesions contracted during childhood.

Both scurvy and rickets are much less frequently encountered in Manila than would be expected from the habits and faulty feeding customs of the people, and these diseases are less frequent in our large clinics than is reported from similar clinics in other parts of the world.

The pathology of these disturbances, their mode of onset, and the course and results are now pretty well known and do not correspond to the conditions found in our smallpox cases sufficiently close to make the danger of mistake in diagnosis a serious consideration.

The close resemblance in the character of the deformities, their constant association with a history of smallpox during early life, and the absence of similar lesions under other conditions seem to warrant the conclusions that the deformities are a complication of variola.

NATURE OF THE LESIONS

The morbid anatomy and histology of the lesions and deformities have been studied in one case by Crowell. (Case III.)

In our preliminary report we stated that:

> The process appears to be due to destructive lesions in the epiphyses of the bones. The shafts of the ulna and radius seem to be normal, except in length. The ends of the bones are enlarged and irregular in shape and similar changes may be encountered in the carpal, metacarpal and phalangeal bones.
>
> The circumferential growth of these bones is not disturbed in the least. There is no sign of underdevelopment in diameter thus proving that the periosteum upon which the circumferential growth depends is not affected.
>
> The bones are markedly shortened and stunted in longitudinal growth, in some cases they are reduced to less than one half the length of the normal bone. The obvious conclusion from this fact is that the seat of the primary lesion is in that part of the bone between the epiphysis and diaphysis which develops actively "ex utero."

Further study of the additional cases reported here with the additional information secured by one autopsy as well as that afforded by Roentgen records apparently confirms the statements made in the preliminary report.

CASE RECORDS

Case I (file and record No. 6992, fiscal year 1912).—V. P., female, Filipina, 27 years old, seamstress, born in Malabon.

She had smallpox during childhood, and as a complication she developed deformity of the left elbow joint, with partial ankylosis and shortening of the bones of the left arm and forearm. (Plate I.)

Case II (file and record No. 5368, fiscal year 1912).—P. B., male, Filipino, born in Mindoro. Had smallpox when a little boy and as a complication he developed deformity of both elbow joints with marked shortening of the bones of the forearms and slightly of the arms, with partial ankylosis of both elbow and wrist joints. Deformity also of both knee joints and some shortening of the bones of both legs. (Plate II and Skiagrams I, II, and III.)

Case III (file and record No. 2464, fiscal year 1912).—A. A., female, single, washerwoman, age 32; born in Silang, Cavite. Had smallpox when a little girl with subsequent deformity of the elbow joints and left wrist, with distinct shortening of the bones of forearms on both sides. Deformity of both knee joints and distinct shortening of the bones of both legs exist. There is a partial ankylosis of the elbow joints. (Plate III, figs. 1 and 2; Plate IV, figs. 1 and 2.)

This patient died March 22, 1912.

Clinical diagnosis: Variola bone lesion; dysentery, acute, bacillary; colitis, chronic, tuberculous; tuberculosis, pulmonary. Autopsy was performed by Crowell, who reports his findings as follows:

Anatomic diagnosis: Pneumonia, lobar, left lower lobe; tuberculosis, chronic pulmonary; hydrothorax, left; pleurisy, chronic obliterative, double; colitis, acute ulcerative; fatty degeneration of liver; pachymeningitis hæmorrhagica interna acuta; adenoma of thyroid, left lobe; dental caries; deformity of long bones.

Body is that of an emaciated, adult Filipina of short stature, being 132 centimeters in length and weighing 21.80 kilograms. Anterior upper teeth are missing, and the two lateral incisors are loose. Inferior molars are carious. Joints are enlarged and flat. The epiphyses of the long bones are enlarged as are their condyles. Bones of the arms and legs are shortened and bent outward. Apparently there is a partial dislocation of the wrist and knee joints. Posterior aspects of both knees are flat. Costal cartilages are curved backward and inward, pulling the sternum backward, so that the chest is flat and shows a slight depression on its anterior midportion. Scars of smallpox are on the body, being especially numerous over the face. Legs pit on pressure. Rigor mortis is marked. Abdomen is depressed and scaphoid. Panniculus adiposus is scant. Tissues are rather dry.

Peritoneum is smooth. Intestines are contracted. Diaphragm reaches the lower border of the fourth rib on the right and fifth on the left.

Thorax.—Left pleural cavity contains about 60 cubic centimeters of yellowish clear fluid. Left lung is adherent posteriorly. Its lower lobe is consolidated with grayish, firm areas over its surface. In the upper lobe there are 3 old nodules of tuberculosis as large as beans. Section through the lower lobe shows a grayish, uniformly firm surface. On pressure a grayish exudate is expressed. Right lung is also adherent to the chest wall, and shows about 7 tuberculous nodules similar to those of the upper left lobe. Bronchi contain grayish exudate. Bronchial glands are intact.

Pericardium is smooth and shining, and contains a normal amount of fluid. Heart is apparently normal in size and consistence. Its chambers contain post-mortem clot. Valves are thin and delicate. Musculature is firm and brownish in color. Aorta measures at the base 5.4 centimeters, at the isthmus 4.4 centimeters, at the cœliac axis 4 centimeters, at the bifurcation 2.6 centimeters. A few calcareous patches are present on the intima of the coronary arteries. Four or five fibrous areas are present on the base of the aorta. Heart weighs 135 grams.

Spleen is moderately firm, apparently normal; weighs 43 grams.

Kidneys apparently normal; weight, 150 grams.

Liver shows extensive fatty degeneration; weighs 654 grams.

Gall bladder and bile ducts are free.

Stomach contains a whitish, clear, viscid fluid. Its mucosa is intact.

Duodenum shows lymphoid tissue very clearly, otherwise normal.

Pancreas is very firm, and cuts with increased difficulty; section shows slight fibrosis.

Adrenals are small; cortex is yellow; medulla dark.

Intestine.—The colon is ulcerated and slightly hæmorrhagic, especially near the rectum. The ulcers are extensive, superficial, not undermined, not ragged. Close to the cæcum are a few small hæmorrhagic, not undermined ulcers. No parasites are found. Peyer's patches and solitary follicles are not prominent. Mesenteric nodes and retroperitoneal nodes are not enlarged.

Urinary bladder contains a small amount of turbid urine. Its mucosa is intact.

Generative organs are apparently normal.

Throat organs.—In the left lobe of the thyroid gland is a well encapsulated, thoroughly enucleable, yellowish colored tumor as large as a walnut. Section shows a yellowish, thick substance contained in the small spaces of the parenchyma of the growth.

Brain.—Between the brain and dura mater is a considerable blood clot. The inner surface of the dura is hæmorrhagic, showing threads of fibrin and masses of clot. The convolutions are prominent, opaque, and there is clotted blood in the fissures. This does not extend to the brain substance. There is an increase of intraventricular fluid. Brain is somewhat softer than normal.

Bones.—The elbow joints are the seat of marked deformities, and they are formed by the normal number of bones: the lower extremity of the humerus on the upper part and the upper ends of the radius and ulna on the lower part. The shafts of these bones are more or less bent on their long axes.

Humerus.—The lower end of this bone shows the following anatomical peculiarities: the capitulum or lateral epicondyle is enlarged; radial depression is very shallow or rather absent; coronoid depression is, however, about normal in size; trochlear ridge is more prominent than normal; median epicondyle is smaller than the lateral; on the outer wall of the olecranon depression is seen a flat oval facet which provides articulation for a cartilaginous process that projects from the outer aspect of the olecranon process. This additional structure determines an incomplete adjustment between the olecranon process and its corresponding depression. The olecranon depression measures 2 by 1.7 centimeters in diameter. Trochlea and radial head measure 2.3 centimeters and 1.6 centimeters in width respectively. The distance between the inner and outer condyles is 5.2 centimeters. The articular surface of the bone is rather thickened.

Ulna.—The upper extremity of this bone presents more remarkable anomalies. The top of the olecranon process is very prominent, convex everywhere rather than rectangular in shape; on the outer aspect of the head is a groove 0.5 centimeter in its transverse diameter, extending from the external side of the olecranon process downward and slightly forward along the outer border of the greater sigmoid cavity to be lost in the broadened bicipital hollow. Just behind this groove is a process with a facet on its anterior aspect, semicircular in shape, and directed forward and outward, its greatest diameter being 8 millimeters in length. The lesser sigmoid cavity is entirely absent. In front, the elongated tongue-like coronoid process projects forward, then upward, describing superiorly and inferiorly a regular curved line. Only the projecting portion of this process measures 2.5 by 2 centimeters in its greatest dimensions. The

inner border of the great sigmoid cavity is more prominent than normal. The great sigmoid cavity itself is broad and transversely divided by a narrow, shallow depression, the normal longitudinal ridge being absent. The tubercle below the coronoid process on the anterior surface of the bone is missing. The olecranon process measures 2.6 centimeters in height, while the coronoid process measures 2.7 centimeters in its anteroposterior diameter.

Radius.—Not less remarkable changes are present in the upper end of this bone. On its anterior surface is a wide, slightly concave, rather quadrilateral facet which articulates with the capitulum of the humerus. This facet measures 1.7 by 1.5 centimeters. On the inner side of the upper end is another semicircular facet which extends from the top of the extremity downward and is directed inward and backward for the articulation with the equally semilunar articular surface located at the outer side of the head of the ulna. This facet measures 1.1 centimeters in its greatest diameter. Back of the upper end of the bone there are more or less irregular projections, the edges of which form an obtuse angle facing downward and inward. The external side of the head is represented by the prominent border of the quadrilateral facet. The neck is more slender than normal and anteriorly flattened, the tuberosity beyond being more prominent than usual.

Knee joint.—In the deformity of this joint the tibia and the fibula are concerned, the femur being apparently well shaped.

The femur bears the normal anatomical characteristics, the only exception is the thickness of the articular surfaces of both condyles which appear to be visibly chondroid. The inner condyle measures 5.8 by 2 centimeters. The outer condyle measures 6 by 2.5 centimeters.

Distance between tuberosities is 7 centimeters.

Distance between inner tuberosity and internal border of outer condyle, 3 centimeters.

Distance between outer tuberosity and external border of outer condyle, 2.5 centimeters.

Intercondylar notch, 2.6 centimeters in width and 2.5 centimeters in depth.

The tibia is the most deformed of the three bones. The condyles of the upper end of the bone are not on the same level, the median condyle being much lower than the lateral. The articular surface of the median condyle is more concave from before backward and from side to side than normally; its edge is rounded anteriorly; the lateral condyle is flat and smaller than the median one; its articular surface is moderately convex from backward and from side to side; at the mid-line the articular surfaces of both condyles fuse together to form a very slight elevation which represents the spine.

Both condyles are markedly inclined backward, overhanging the shaft of the bone so that a prominent projection is formed protruding backward for a distance of 1.5 centimeters. Located inferiorly and laterally is an irregular semicircular facet on the edge of the median condyle to be articulated with a similar facet on the head of the fibula. In front is a transverse, oval tubercle. On both sides, the condyles overhang the shaft. The articular surface measure 6.5 by 4.5 centimeters. Distance between the tuberosities is 7.2 centimeters. The whole articular surface is also apparently cartilaginous.

The head of the fibula is considerably changed in its external architecture. The summit of it is convex externally from before backward and concave exteriorly from side to side. Located anterolaterally is an articular surface which provides articulation for the lateral condyle of the tibia. The inner side of the head is represented by a vertical ridge, terminating below in a sharply pointed process 0.5 centimeter in length. Anteriorly is a convex, slightly elevated surface partially overhanging the shaft of the bone. Posteriorly is a straight ridge which extends from the styloid process obliquely outward. Externally is a tuberosity formed by the union of the posterior ridge and the anterior rounded edge or convex portion of the head. This tuberosity is very prominent, rounded, smooth, and visibly chondroid in consistence.

Summarizing the conditions in the bones above described, it is apparent that the diaphyses of the bones are shorter than normal and that the ends of the bones, representing the original epiphyses, are much altered in configuration. In the shafts of the bones which were removed for examination there is no apparent change from normal in contour or diameter. Mesial longitudinal section through the ends of the bones shows complete ossification of the epiphyseal extremities, and no indication of the line of junction between the epiphyses and diaphyses is present. The deformities of the epiphyses must, therefore, have occurred before the period of full growth, and the interference with the longitudinal growth of the diaphyses must have been due to some disturbance at the line of junction with the epiphyses.

As is to be expected from the above description of the condition of the bones, examined at a period after the cessation of active disease and after healing has taken place, the microscopic examination of the bones shows nothing which will further elucidate the nature of the active process. Complete ossification has taken place, and decalcified sections of the bones show no alterations from the normal condition of bone growth at this period of life. The epiphyseal line of growth is obliterated, and the compact bone and marrow bear normal relations. The only alteration is in the size and conformation of the epiphyses.

Case IV (file and record No. 1367, fiscal year 1912).—J. M., male, Filipino, single, carpenter, 23 years old. Had smallpox when a little child, as a result of which he developed deformity of the left knee, with partial ankylosis and some shortening of the femur. There also is deformity of the toes of the left foot, with shortening of the phalanges, and of both elbow joints with partial ankylosis and shortening of the bones of forearms on both sides. (Plate V, figs. 1 and 2.)

Case V (file and record No. 3611, fiscal year 1912).—C. E., female, Filipina, 29 years old, born in Manila.

Had smallpox when a little child, as a result of which she developed deformity of both knee and elbow joints, with slight ankylosis and some shortening of the bones of legs and forearms. (Plate VI, figs. 1 and 2.)

Case VI (*file and record No. 2187, fiscal year 1912*).—J. F., male, Filipino, about 27 years old, water carrier, born in Manila.

Had smallpox when a little child, as a result of which he developed deformity of both elbow joints and wrist and finger joints, right hand, with partial ankylosis of corresponding joints and shortening of the right humerus and some of the carpal and phalangeal bones of the right hand. (Plate VII, fig. 1.)

Case VII (*file and record No. 2594, fiscal year 1912*).—J. A., male, Filipino, 18 years old, student, born in Iloilo.

Had smallpox at the age of 15 and developed as a complication deformity of both elbow and knee joints of both sides, with very little ankylosis and some shortening of the bones of the arms and forearms. (Plate VII, fig. 2; Plate VIII, figs. 1 and 2; and Skiagram IV.)

Case VIII (*file and record No. 2967, fiscal year 1912*).—J. M., male, Filipino, laborer, 40 years old.

Had smallpox when a child, as a result of which he developed deformity of both elbow joints, with partial ankylosis, and shortening of the bones of arms and forearms. (Plate IX, figs. 1 and 2.)

Case IX (*file and record No. 4741, fiscal year 1912*).—I. G., female, Filipina, housekeeper, 54 years old, born in Gapan, Nueva Ecija.

Had smallpox when a little child complicated by arthrites and subsequent deformity of both wrist joints, with partial ankylosis and shortening of some of the carpal bones and phalanges of the right hand. (Plate X, fig. 1.)

Case X (*file and record No. 5050, fiscal year 1912*).—S. C., male, Filipino, laborer, 26 years old, born in Tondo, Manila.

Had smallpox when a little boy, followed by deformity of both wrist joints with partial ankylosis, but no apparent shortening of the bones, nor diminution in diameter except malformation in the articular and in the elbow joints, especially of the bones of forearms. (Plate X, fig. 2.)

Case XI (*out-patient service*).—A. H., male, Filipino, 35 years old, laborer, born in Taal, Batangas.

Had smallpox at the age of 2, as a result of which he developed ankylosis of temporomaxillary joints with deformity of the left ramus of the lower mandible, consisting of diminution in length and certain irregularities along its anterior surface. There is complete ankylosis of the left elbow joint and deformity of the lower end of the humerus, with shortening of this bone.

There also is shortening of the bones of the forearms. (Plate XI, figs. 1 and 2.)

The biceps, triceps, brachialis anticus, and deltoid muscles are atrophied.

An interesting feature of the case is the presence of a slit-like opening between the left incissors through which the patient takes food, it being impossible for him to open his mouth because of the ankylosis of the jaw.

Case XII (*out-patient service*).—V. P., male, Filipino. Had smallpox when a child, and as a complication he developed deformity of the wrist and elbow joints in the right arm, with shortening of the bones of the forearms. (Skiagram V.)

ILLUSTRATIONS

PLATE I

Case I, showing deformity of the left elbow joint, with partial ankylosis and shortening of the bones of left arm and forearm.

PLATE II

Case II, showing deformity of both elbow joints with marked shortening of the bones of the forearms and slightly of the arms, with partial ankylosis of both elbow and wrist joints. Deformity also of both knee joints and some shortening of the bones of both legs.

PLATE III

Case III, showing deformity of the elbow joints and left wrist, with distinct shortening of the bones of forearms. There is a partial ankylosis of the elbow joints.

PLATE IV

Case III, showing deformity of both knee joints and distinct shortening of the bones of both legs.

PLATE V

Case IV, showing deformity of the left knee, with partial ankylosis and some shortening of the femur. There also is deformity of the toes of the left foot, with shortening of the phalanges,. and of both elbow joints with partial ankylosis and shortening of the bones of the forearms.

PLATE VI

Case V, showing deformity of both knee and elbow joints, with slight ankylosis and some shortening of the bones of legs and forearms.

PLATE VII

Fig. 1. Case VI, showing deformity of both elbow joints and wrist and finger joints, right hand, with partial ankylosis of corresponding joints and shortening of the right humerus and some of the carpal and phalangeal bones of the right hand.

2. Case VII, showing deformity of both elbow and knee joints of both sides, with very little ankylosis and some shortening of the bones of the arms and forearms.

PLATE VIII

Same case as Plate VII, fig. 2.

PLATE IX

Case VIII, showing deformity of both elbow joints, with partial ankylosis and shortening of the bones of arms and forearms.

PLATE X

Fig. 1. Case IX, showing complication by arthritis and subsequent deformity of both wrist joints, with partial ankylosis and shortening of some of the carpal bones and phalanges of the right hand.

2. Case X, showing deformity of both wrist joints with partial ankylosis, but no apparent shortening of the bones, nor diminution in diameter except malformation in the articular and in the elbow joints, especially of the bones of forearms.

PLATE XI

Case XI, showing ankylosis of temporomaxillary joints with deformity of the left ramus of the lower mandible, consisting of diminution in length and certain irregularities along its anterior surface. There is complete ankylosis of the left elbow joints and deformity of the lower end of the humerus, with shortening of this bone.

SKIAGRAMS I–III

(See Plate II.)

SKIAGRAM IV

(See Plate VIII.)

SKIAGRAM V

Case XII, showing deformity of the wrist and elbow joints in the right arm, with shortening of the bones of the forearms.

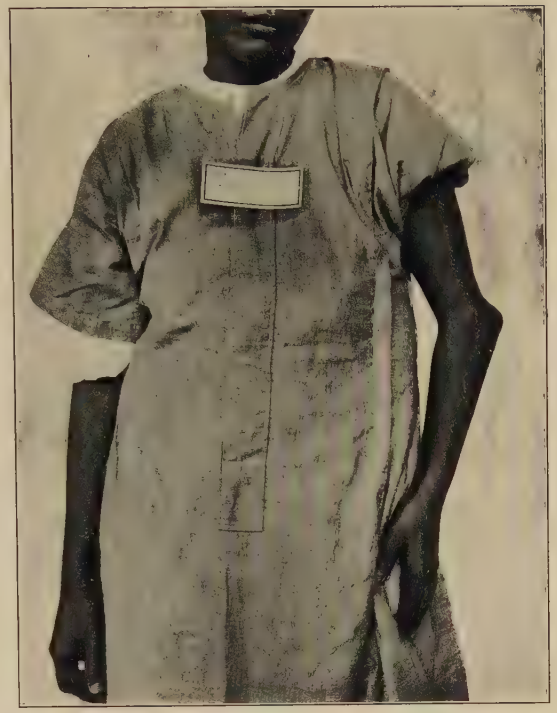


Fig. 1.

Fig. 2.

PLATE I. CASE I. DEFORMITY OF LEFT ARM AND FOREARM.

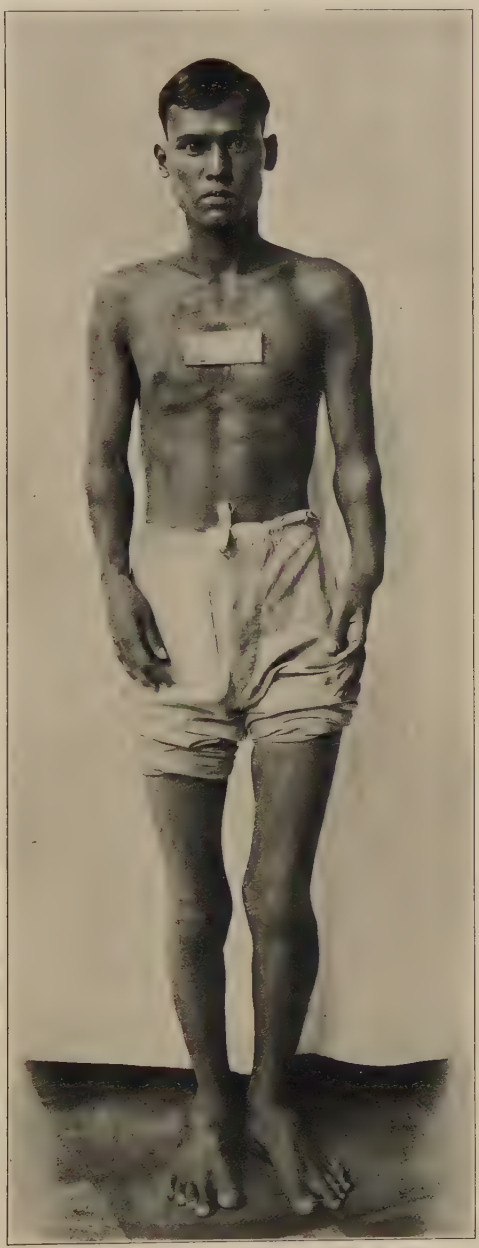


PLATE II. CASE II. DEFORMITIES OF ARMS AND LEGS.

Fig. 1.

Fig. 2.

PLATE III. CASE III. DEFORMITY OF UPPER EXTREMITIES.

Fig. 1.

Fig. 2.

PLATE IV. CASE III. DEFORMITY OF BOTH LEGS.

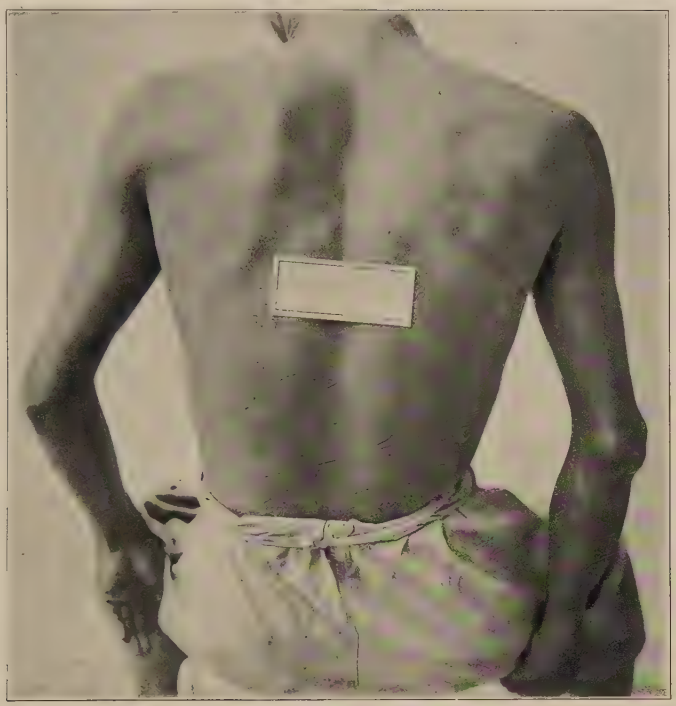


Fig. 1. Case IV. Deformities of upper extremities.

Fig. 2. Case IV. Deformities of left leg and foot.

PLATE V.

Fig. 1. Case V. Deformity of upper extremities.

Fig. 2. Case V. Deformity of lower extremities.

PLATE VI.

Fig. 1. Case VI. Deformity of upper extremities.

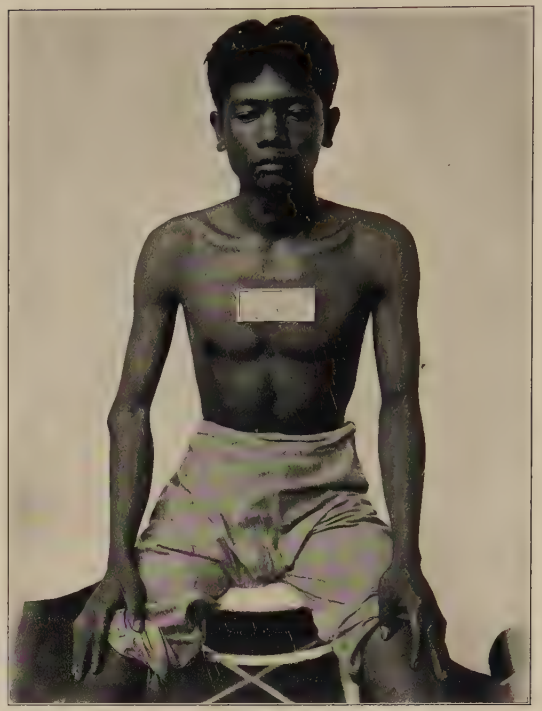


Fig. 2. Case VII. Deformity of upper extremities.

PLATE VII.

Fig. 1. Case VII. Deformity of knee joints.

Fig. 2. Case VII. Deformity of upper extremities.

PLATE VIII.

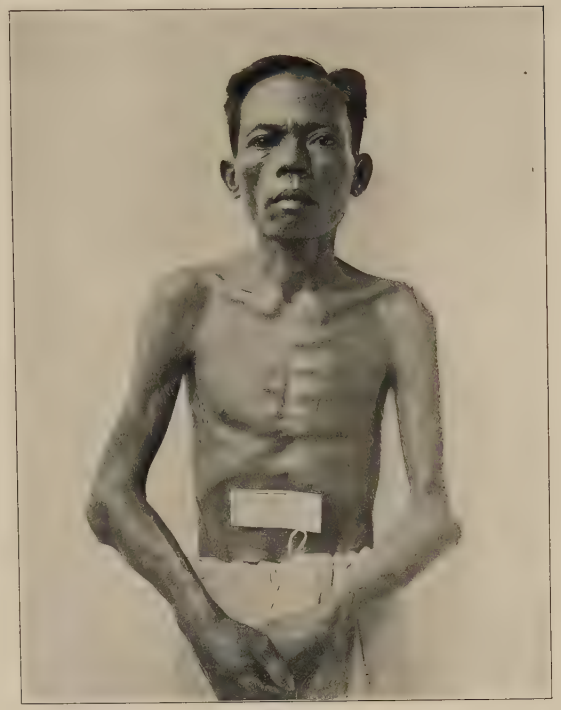


Fig. 1.

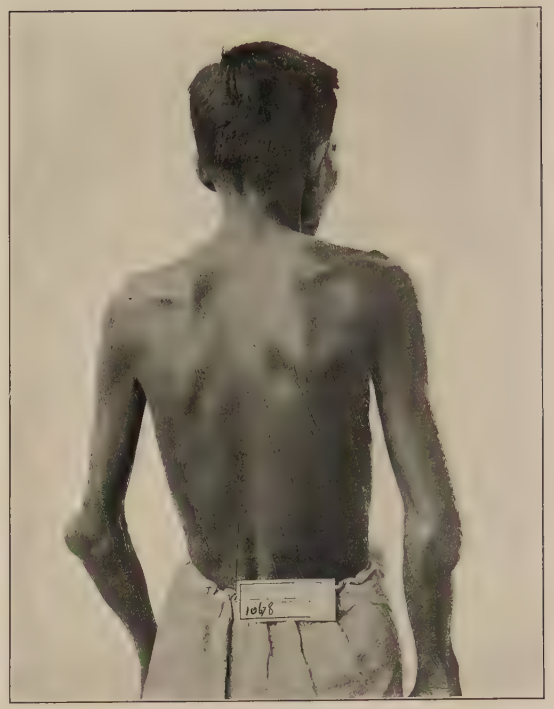


Fig. 2.

PLATE IX. CASE VIII. DEFORMITY OF UPPER EXTREMITIES.

Fig. 1. Case IX. Deformity of both wrist joints, and bones of right hand.

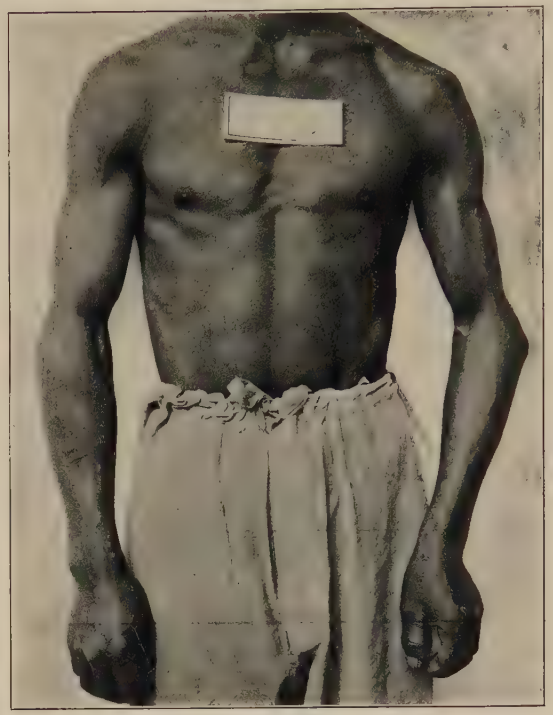


Fig. 2. Case X. Deformity of upper extremities.

PLATE X.

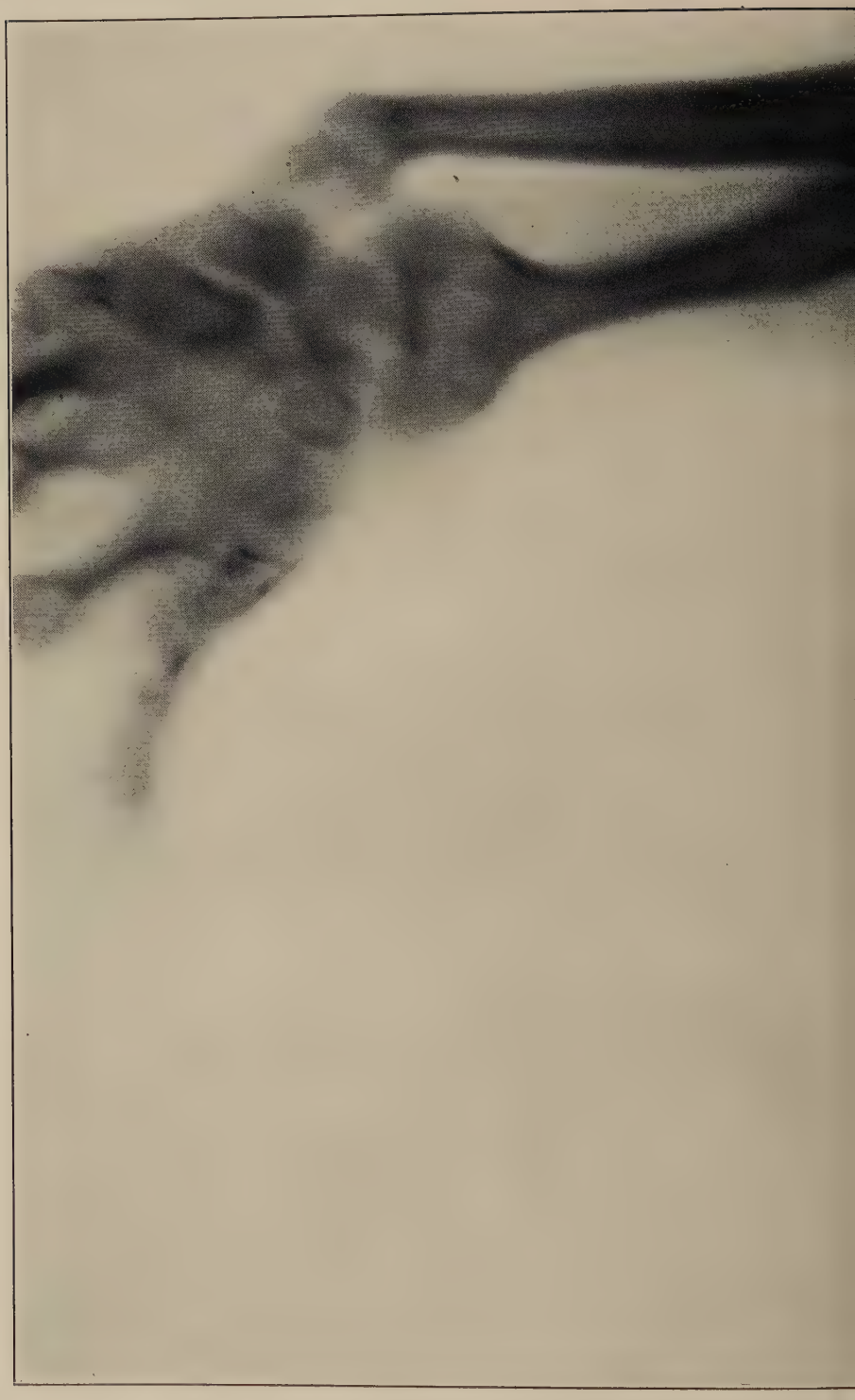
Fig. 1. Case XI. Deformity of facial bones and bones and joints of left arm.

Fig. 2. Case XI. Deformity of left arm.

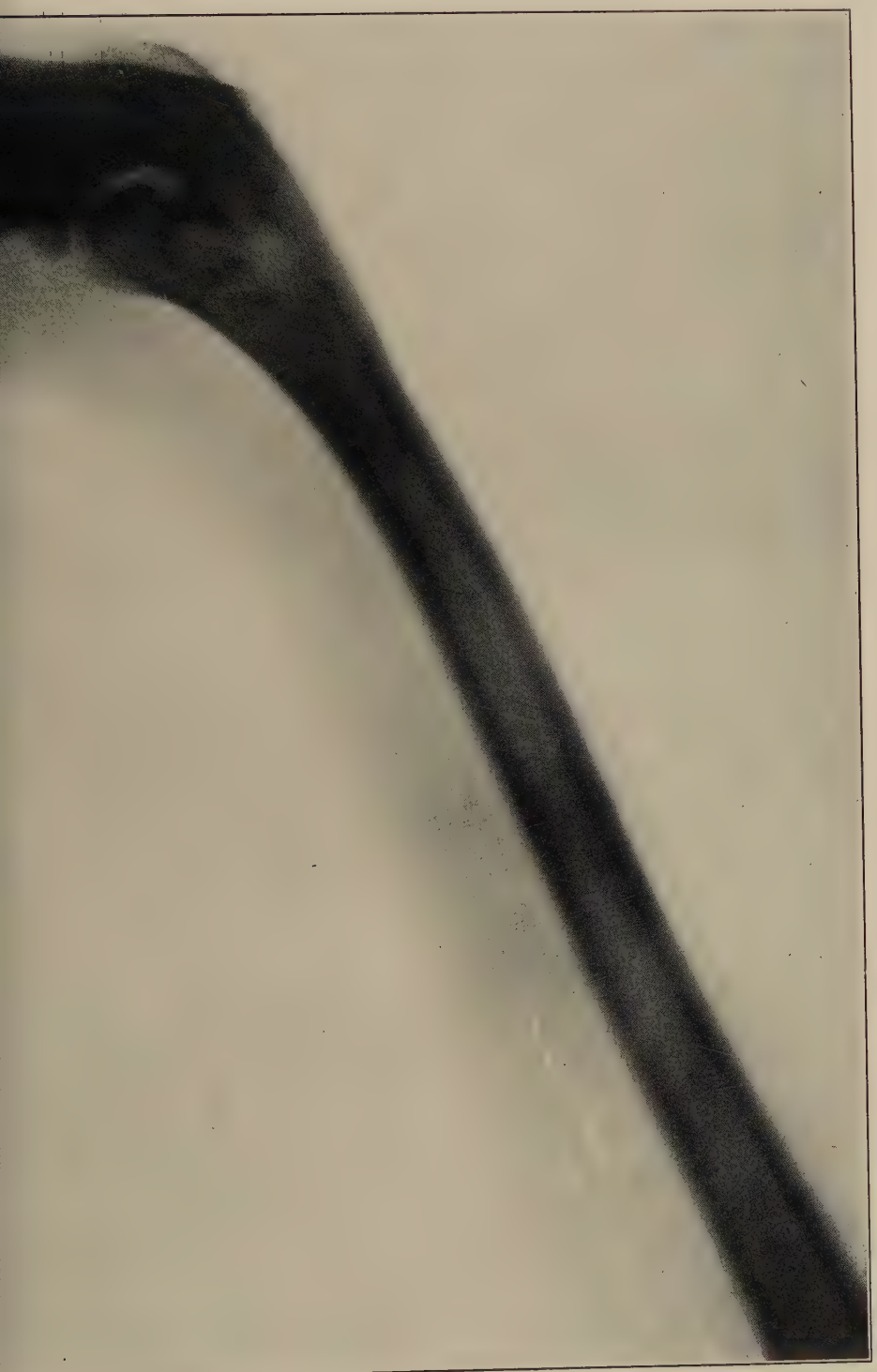
PLATE XI.

SKIAGRAM I. A

OF WRIST JOINTS.



SKIAGRAM II. ANKYLOSIS OF ELBOW AND WRIST J



ITH MARKED SHORTENING OF BONES OF THE FOREARM.

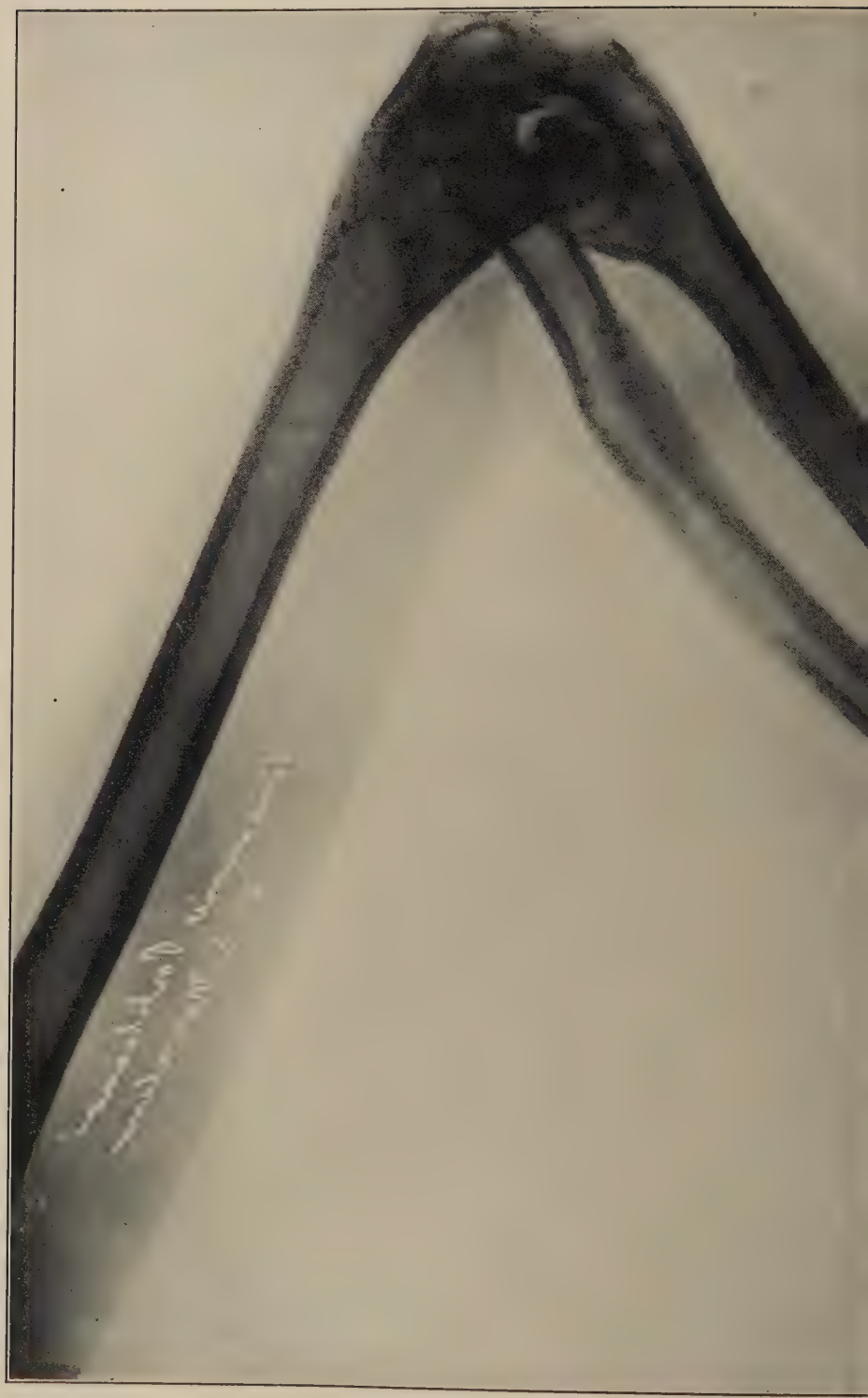
SKIAGRAM III

LOSIS OF WRIST JOINTS.

SKIAGRAM IV. DEFOR

Diagram IV.

F ELBOW AND KNEE JOINTS.



SKIAGRAM V. DEFORMITY OF THE WRIST AND ELBOW JOINTS

IGHT ARM, WITH SHORTENING OF THE BONES OF THE FOREARM.

STATUS THYMICO-LYMPHATICUS AMONG FILIPINOS [1]

By B. C. Crowell[2]

(*From the Biological Laboratory, Bureau of Science, Manila, P. I.*)

Two plates

The term "lymphatism" is about as old as that of "scrofula," and for many years it conveyed an idea about as indefinite. As the advances in our knowledge of human diseases and their causes have practically abrogated the use of the latter term, its place being taken by a more definite nomenclature, so have the conditions suggested by the older term lymphatism been more accurately defined, the conditions associated with it been more closely circumscribed, and the interpretations of the anatomical changes become more elaborate.

To the older school the term lymphatism conveyed an indefinite idea of an individual with a pasty, sallow skin, flabby subcutaneous tissues, poorly developed musculature, a tendency to hyperplasia of the lymphatic organs, and a vulnerable glandular system.

The object of this paper is to trace briefly the steps by which our knowledge of this condition has become more accurate, to show that the entity, which has evolved from this indefinite conception, namely, status thymico-lymphaticus, occurs with considerable frequency in the Philippine Islands, and that here it has one unusual feature in that it has given rise to confusion with at least one condition frequently encountered here.

Whitmore(1) in 1911 reported 16 cases showing various grades of status lymphaticus out of a series of 565 autopsies performed in India. As far as ascertained, this is the only record of such cases in the Orient. He remarked that the condition is in no way dependent on race or environment.

It has long been recognized that sudden death is not an infrequent occurrence in persons of this type, and the almost

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constant presence of an enlarged thymus gland, coupled with the clinical evidence of respiratory embarrassment in many cases, has led many authors to claim that direct mechanical pressure of the thymus is accountable for the sudden death. Thus has arisen the much discussed question of the so-called "mors thymica." The mechanical pressure of the thymus has been claimed by some to be exerted on the trachea, by some on the heart, by others on the vessels, and by still others on the nerves. Pressure on the trachea, however, has attracted most attention, and at the present day there are still many who claim evidence of such a manner of death.

It may here be said that the standard for the size of the thymus has been very unsatisfactory, and comparatively recent work has shown that many glands which were accounted enlarged were but normal. The old idea that the thymus diminished in weight from the second year of extra-uterine life is now replaced by the certain knowledge that in normal individuals it increases in weight up to about the fifteenth year, after which it normally undergoes gradual involution. The thymus, however, suffers so severely as the result of nutritional disturbances that it has been said that the condition of the thymus is the best single indicator of the state of nutrition of the body. This alteration in the thymus as the result of general acute or chronic disease was termed "accidental involution" by Hammar,(2) and the recognition of this has played a very important part in the interpretation of statistics.

The evidence adduced to show that the thymus exerts sufficient pressure to produce suffocation is not all convincing and Wiesel's(3) conclusion that there may be a few cases dying from this cause, while the majority are not thus accounted for, seems justifiable. The fact that many infants who had large thymus glands died with symptoms of stridor or laryngismus and presented on superficial anatomical examination little else to explain the death is accountable for the importance attached to the large thymus. As long ago as 1858, Friedleben(4) investigated many of these cases and issued the dictum, "Es gibt kein Asthma thymicum," but it remained for Paltauf in 1889(5) to promulgate the theory that the enlarged thymus was only one evidence of a general vulnerable bodily constitution which he designated "status lymphaticus." He described patients with this condition as exhibiting "great pallor of the skin, usually a well developed panniculus adiposus, more or less congested organs without special changes in consistence; the spleen is mostly

enlarged and shows prominent follicles; in the epiphyseal cartilages are found evidences of active rachitic proliferation; the follicles of the lymphatic glands are much enlarged and the thymus well developed." He recognized the general lymphatic changes which are present, and the cardiovascular hypoplasia, and summarized the whole as evidence of a "lymphatic-chlorotic constitution." The cause of death he considered to be due to this anomalous constitution of the body, and the enlarged thymus was for him but a symptom of that general nutritional disturbance which was further evidenced by the enlarged lymphatic glands, tonsils, etc.

Bartel,(6) in Weichselbaum's laboratory, added another idea in his conception of the lymphatic changes and those which he found frequently associated with them as evidence of a "status hypoplasticus"; the associated changes found were anomalies of development in other organs, as hypoplasia of the arterial system and the genitalia, syringomyelia, hydrocephalus, glioma, and frequently horse-shoe kidney, and embryonic lobulation of the kidneys and lungs.

Very few ideas have been added to those of Paltauf and Bartel in the interpretation of the findings in such cases. The conditions under which they are found, and the diseases with which they are associated, however, have been much elaborated, and some authors, especially Von Neusser,(7) have indicated certain external appearances of the body which assist in making the diagnosis clinically.

This condition occurs in both infants and adults, although it is more easily recognized in the latter class. It is now well known that persons who are subjects of this condition have a peculiarly vulnerable constitution and are liable to death from seemingly insufficient causes. The cause of death in these cases is still a matter of much discussion, but Paltauf's contention that death is due to a paralysis of the heart is fairly generally accepted. Shridde's(8) hypothesis that death is due to a kind of endogenous poisoning through excessive or disordered function of the thymus Wiesel considers to be based on insufficient evidence. Wiesel(9) himself has noted an hypoplasia of the chromaffin system in cases of status lymphaticus, and this undoubtedly is an important element acting through the production of diminished tone of vessels and nerves.

All grades of the condition are found and are termed variously status thymicus, status lymphaticus, status thymico-lymphaticus, and partial status lymphaticus. It is possible and not improb-

able that there are two classes of cases; one in which the condition is a pure status lymphaticus in the sense of Paltauf, and another in which the various changes are more or less caused by the disease with which they are associated.

Kolisko(10) has given the best description of the anatomical conditions found in cases of pure status lymphaticus, while Von Neusser(7) has probably furnished the best data on which to base a clinical diagnosis.

For the diagnosis of status lymphaticus in the cadaver, Kolisko has given the following signs:

1. The failure of the involution of the lymphatic organs which otherwise occurs regularly at puberty. The enlarged tonsils consist of lymphoid tissue while their epithelial crypts are small; the follicles at the base of the tongue cause by their enlargement a rough granular condition of that part, the upper part of the pharynx is beset with lymphoid nodules as large as peas, mostly in the pharyngeal vault, but also on the posterior pharyngeal wall, in the pyriform sinuses, and even in the larynx on the inner side of the epiglottis.

2. The cervical lymphatic glands are bean-size to, at the most, cherry-size, tolerably firm and mostly pale, sharply circumscribed one from the other.

3. The thymus persists beyond puberty, and frequently undergoes hyperplasia.

4. The endocardium of the left ventricle shows a diffuse cloudiness on the valves, the mural endocardium, and in the heart muscle, without inflammatory manifestation. The alterations in the lining of the heart lead Kolisko to conclude that abnormal pressure with a tendency to dilatation has been acting on the ventricular endocardium.

5. The enlarged spleen shows hyperplastic follicles on the cut surface, and its capsule is tense and often very friable.

6. The mucosa of the intestine shows distinct hyperplasia of the follicles, and the mesenteric lymphatic glands are proportionately enlarged. So are all other lymphatic glands of the body enlarged in various degrees, the smaller being mostly rich in blood, the larger bloodless and not juicy.

7. The bone-marrow frequently exhibits the appearance of medulla rubra.

8. As the size and weight of the thymus normally are subject to remarkable alterations and as the other lymphoid tissue of the child's organism is so variable in its growth, and hyperplasia of it is so frequent as the result of inflammatory irritation or disturbances of nutrition as in rickets, it is clear that the interpretation of the pathologico-anatomical findings in relation to the diagnosis of status lymphaticus in the cadavers of children up to the sixth year is beset with extraordinary difficulties. Therefore, for diagnostic purposes one must emphasize the occurrence of the size of the thymus, disproportionate to the age of the child, as well as the frequency and similarity of the hyperplasia in the lymphatic system, and also the condition of nutrition must be borne in mind.

9. A frequent, but not constant, finding is the narrowness and delicacy of the aorta and the rest of the arterial system, yet hypoplasia of the arteries can exist even without a macroscopically recognizable hyperplastic lymphatic system. Also, the hypoplasia of the genitals often accom-

panying the hypoplasia of the arteries is no constant phenomenon in the lymphatic constitution. The aorta as well as the peripheral arteries show an unusual narrowness, with thin walls and abnormal elasticity to such a degree that a section of vessel after removal retracts to almost half its original length.

10. In the heart sometimes a surprising smallness (hypoplasia) is encountered, but the heart can also be of normal size or even hypertrophic. The hypoplasia of the arterial vascular system is possibly commensurate with the abnormal blood pressure in such individuals, and stands apparently in relation to the hypoplasia of the adrenals and chromaffin system found by Wiesel in many cases.

Von Neusser's work has been consulted in preparing the following description of the clinical appearance of such cases, but his work was practically confined to adults, while Escherich(11) and Howland(12) have furnished data for the diagnosis in children. It goes without saying that one who is on the lookout for such cases and who is familiar with their appearance and with the diseases with which they are associated will recognize them more frequently than one not so prepared. On account of the relative obscurity of the findings this prepared mind is of more importance in the detection of this disease than of many others.

In males the individuals are usually well nourished and gracefully molded, with smooth velvety skin. The features are not infrequently of the classic type, and the neck rather columnar in shape, being set rather abruptly upon square shoulders without the usual sloping. The extremities are gracefully constructed, and the thighs are rounded and usually arched or rounded both anteriorly and laterally. The hair is scant, including the beard and mustache, thoracic and axillary, abdominal, pubic, and that over the extremities. The pubic hair is usually cut straight across as in the female. In fact, the whole is practically a feminine type of body.

The female, on the other hand, while preserving in part the graceful feminine outlines of the body, and having for the most part the same scantiness of hair, frequently presents heterosexual characteristics, with deep base voice and some beard and mustache.

The diseases with which it is most frequently associated are those of the ductless glands, as in Addison's and Basedow's diseases, acromegaly, osteomalacia, and in brain tumors, and in anomalies of the sexual organs such as hermaphroditism. In Basedow's disease it is very frequent, and it is considered by Shridde(8) and many others that the lymphocytosis which is so frequent in Basedow's disease is dependent upon the lymphatic

constitution and that a lymphocytosis of more than 40 per cent is a contraindication for operation. Many investigators, especially those of the French school, have gone so far as to attribute the symptoms of Basedow's disease to the disordered function of the thymus and to treat by thymectomy rather than thyroidectomy. Thymus feeding in such cases has not been uniformly successful. However, in view of the frequent fatalities following thyroidectomy in exophthalmic goitre, advanced or extensive lymphatic and thymus change should be excluded as far as possible by differential blood count, roentgenization, and percussion of the thymus region. Capelle(13) collected statistics from the literature in regard to the association of status thymico-lymphaticus and Basedow's disease, as follows: Of patients with Basedow's disease dying of intercurrent infections, 44 per cent showed hypertrophic thymus; of those dying purely from Basedow's without associated disease this became 82 per cent, and of those dying at or after operation 92 per cent, while if those were excluded who died from hæmorrhage it became 100 per cent. He, therefore, concluded that the thymus enlargement was practically an indicator of the severity of the disease.

But certainly not all cases of status thymico-lymphaticus are associated with such extensive alterations in other ductless glands, and the anatomical records of homicides and suicides are particularly interesting. These have been studied by many workers, from two of whom I shall quote.

Bartel(14) in 1910 studied 122 cases of suicides, and out of 52 cases found—

	Per cent.
Status thymico-lymphaticus in	36
Status lymphaticus in	26
Partial status lymphaticus in	20
and had incomplete protocols in	18

Miloslavich(15) studied, in 1912, 110 cases of suicides among soldiers, and found 80 per cent with a lymphatic constitution as follows:

	Per cent.
Status thymico-lymphaticus	47
Status lymphaticus	21
Status thymicus	8.5
Partial status lymphaticus	3.5
Negative as to status	20

Bartel considered lymphatism as a certain and very pregnant sign of a constitutional anomaly, and Miloslavich considered its presence in suicides evidence of mental instability.

REPORT OF CASES

In a series of 300 autopsies, there have occurred 20 cases of well-marked grades of this condition as follows:

	Cases.
Status thymico-lymphaticus	13
Status lymphaticus	7

In addition there have been very numerous cases of lesser grades of lymphoid hyperplasia of the various viscera. It may here be stated that the autopsy service which includes these cases is derived from a large general hospital, a hospital for contagious diseases, and the medico-legal cases occurring in the city of Manila, so that all classes of cases are encountered.

A more detailed examination of these cases follows.[3]

I. CASES OF STATUS THYMICO-LYMPHATICUS

1. (1948.) One case was in a male, 8 years old, whose duration of illness is given as one day, and the clinical diagnosis was undetermined. He had a thymus weighing 27 grams, and hyperplasia of the lymphoid tissue of the pharyngeal ring, spleen, intestine (duodenum, ileum, and colon), and lymphatic glands (mesenteric, femoral, inguinal, and axillary). There were also ecchymoses on the pleura and epicardium, and small external genitalia.

2. (2000.) One case was in a 30-year-old male who died soon after partial thyroidectomy performed under local anæsthesia for the relief of symptoms of Basedow's disease. He had a 40-gram thymus and hyperplasia of the lymphoid tissue of the pharyngeal ring and intestine (ileum and colon).

3. (2011.) A 10-year-old boy died as the result of an automobile accident which caused extensive fractures of the skull. He had a 26-gram thymus and hyperplasia of the lymphoid tissue of the pharyngeal ring, œsophagus, stomach, intestine (duodenum, ileum, and colon), and the cervical and mesenteric lymphatic glands. The adrenals were hypoplastic, and there were ecchymoses on the pleura and epicardium.

4. (1979.) A 12-year-old boy died from drowning. He had a 37-gram thymus and hyperplasia of the lymphoid tissue of the pharyngeal ring, spleen, intestine (duodenum, ileum, and colon), mesenteric, inguinal, and axillary lymphatic glands.

[3] Cultures from the viscera of the cases were sterile unless otherwise stated.

The adrenals were hypoplastic, and there were ecchymoses on the leptomeninges.

5. (1980.) A 7-year-old boy died of streptococcus septicæmia, the duration of his illness being given as three days. The fever in this case along with the enlargement of the superficial lymphatic glands led to the clinical diagnosis of probable bubonic plague. He had a 30-gram thymus and hyperplasia of the lymphoid tissue of the pharyngeal ring, intestine (duodenum and ileum), mesenteric, inguinal, axillary, and cervical lymphatic glands. Epicardial ecchymoses were also present.

6. (1982.) A 9-year-old boy died with slight broncho-pneumonia, the duration of illness being given as twelve days. He was also suspected of having plague for the same reasons mentioned in the previous case. He had a 40-gram thymus and hyperplasia of the lymphoid tissue of the pharyngeal ring, spleen, and inguinal and axillary lymphatic glands.

7. (971.) A 25-year-old male, whose duration of illness could not be ascertained and on whom no clinical diagnosis could be made, had chronic pulmonary tuberculosis with hæmorrhage. He also had a 22-gram thymus and hyperplasia of the lymphoid tissue of the pharyngeal ring, intestine (ileum and colon), and mesenteric, retroperitoneal, and femoral lymphatic glands.

8. (1920.) A 3-year-old boy, who was ill six days with undetermined diagnosis, had slight pleural and intestinal tuberculosis. In addition, he had a 50-gram thymus and marked hyperplasia of the lymphoid tissue of the pharyngeal ring, intestine (duodenum, ileum, and colon), spleen, and inguinal and femoral lymphatic glands. Epicardial, pleural, and gastric ecchymoses were also present.

9. (1845.) Another 3-year-old boy, who was said to have been ill fourteen hours, had general glandular and intestinal tuberculosis. In addition, he had a 25-gram thymus and hyperplasia of the lymphoid tissue of the tonsils, spleen, and intestine.

10. (1761.) A 1-year-old male, ill two hours, supposed to have had nephritis and rachitis, had an "abnormally enlarged" thymus, hyperplasia of the lymphoid tissue of the pharyngeal ring, spleen, intestine, and mesenteric lymphatic glands. He had also a dilated heart and rachitis.

11. (1901.) A 7-year-old boy, who was ill three days and died suddenly, had a "large" thymus, hyperplasia of the lymphoid tissue of the pharyngeal ring and spleen, and an acute gastro-enteritis.

12. (1894.) A 19-year-old male, who died after three days' illness with bubonic plague, had in addition to the lesions attributable to plague a "large" thymus and an hypoplastic aorta and lymphoid hyperplasia in the intestines. *Bacillus pestis* was isolated from this case.

13. (2114.) A 6-year-old male, whose duration of illness was given as four days and on whom a diagnosis of probable grippe was made, had a 37-gram thymus, hyperplasia of the lymphoid tissue of the pharyngeal ring, intestine, mesenteric and superficial lymphatic glands, acute suppurative otitis media, and chronic fibrous pleurisy. A Gram-positive diplococcus resembling a pneumococcus was found in films from the left middle ear. Cultures from the spleen were negative.

II. CASES OF STATUS LYMPHATICUS

14. (1933.) A 2½-year-old girl, who was ill one hour with undetermined diagnosis, had a slight enteritis, hyperplasia of the lymphoid tissue of the pharyngeal ring, spleen, intestine, and mesenteric lymphatic glands, dilatation of the right ventricle, and congestion and œdema of the lungs. The thymus was of normal size.

15. (1929.) A 7-year-old boy, who was said to have been ill thirty minutes with undetermined diagnosis, had a 13-gram thymus and hyperplasia of the lymphoid tissue of the pharyngeal ring, spleen, mesenteric lymphatic glands, and intestine (ileum and colon), slight acute enteritis, dilatation of the right ventricle, and an "unusually small" thyroid.

16. (1799.) A 15-month-old female, whose duration of illness and clinical diagnosis were unknown, had an 18-gram thymus and hyperplasia of the lymphoid tissue of the pharyngeal ring, spleen, intestine, and mesenteric lymphatic glands. In addition, there were ecchymoses in the pleura and duodenum, and no other gross pathological phenomena aside from congestion of the kidneys.

17. (1764.) A 5½-year-old girl, who had numerous fractures from collision with a trolley car, had a 12-gram thymus and hyperplasia of the lymphoid tissue of the pharyngeal ring, spleen, and intestine.

18. (1767.) A 17-year-old female, who was ill ten days after parturition and was supposed to have had acute beriberi, had a cyst of the pituitary gland, a small thymus, and hypoplastic

aorta, hyperplasia of the lymphoid tissue of the pharyngeal ring and spleen, and hypoplasia of one adrenal.

19. (1522.) A 4½-month-old female, who was ill a month with what was diagnosed infantile beriberi, had slight lobular pneumonia, congestion of the kidneys, a 5-gram thymus, anomalous lobulation of one lung, and hyperplasia of the lymphoid tissue of the spleen, intestine, and mesenteric lymphatic glands.

20. (1275.) An 18-year-old female, who was said to have been ill two weeks and whose record does not show the manner of death, had a "small" thymus, hypoplasia of the heart, aorta, and adrenals, hyperplasia of the lymphoid tissue of the pharyngeal ring, spleen, and mesenteric lymphatic glands, a calcific nodule on the pleura, localized atheroma of the aorta, pulmonary congestion, and œdema and parenchymatous degeneration of the kidneys.

Analyses of these cases shows the following features of interest:

1. In 3 cases (1, 16, 20) no essential lesions were found save those of status thymico-lymphaticus.

2. The condition was encountered in 3 cases (3, 4,, 17) of accidental death.

3. In 7 cases (6, 8, 11, 13, 14, 15, 19) the other anatomical lesions which should be considered as contributing factors to the cause of death were slight.

4. In 4 cases (5, 7, 9, 12) there were definite anatomical lesions sufficient to cause death, which were evidently unrelated to status lymphaticus and on which the lymphoid hyperplasia could scarcely be considered dependent.

5. In 2 cases (2, 18) there were definite anatomical lesions in other ductless glands, and in 1 case (10) there was a definite disease due to metabolic disturbance.

6. The cases occurred between the ages of 1 and 30 years, 14 being below the age of puberty.

7. In 6 cases (1, 3, 4, 5, 8, 16) there were encountered ecchymoses on serous surfaces, and in 2 cases (8, 16) on mucous surfaces such as are found in beriberi; and doubtless had the records been more complete, the number of these would be greater.

8. The distribution of the lymphoid hyperplasia is not constant, different organs being affected in various grades in the different cases.

9. There occurred definitely recognizable hypoplasia of the adrenals 4 times (3, 4, 18, 19), of the aorta twice (18, 19), of the

heart once (19), of the thyroid once (15), and of the external genitals once. Careful measurements of the heart and aorta were not made in all cases, and these figures probably do not represent the true state of affairs. This question will be more carefully investigated at another time, but my opinion is that the size of the aorta was below normal in the majority of these cases.

10. The duration of illness was brief in all but 4 cases (6, 18, 19, 20).

It is not proved nor believed that the lymphatic constitution is of greater frequence among Filipinos than among other races, but it is desired to draw attention to its occurrence and to the importance of its recognition. In children its manifestations are the same as in other races; on the other hand, in a large number of adults of the Oriental races the growth and distribution of the hair differs so essentially from that in Caucasian races that the same importance cannot be attached to this point in diagnosis as is given it by those whose investigations do not include Orientals. I refer to the almost complete absence of beard, mustache, axillary and thoracic hair, and that on the extremities which is common among Orientals. Also, in tropical climates where acute and chronic infections of the skin of the lower extremities are so frequent on account of the custom of the natives of going barefooted, enlargement of the femoral and inguinal glands of inflammatory origin is very frequent, and enlargements of this type should not lead to the diagnosis of the lymphatic constitution. However, during the recent period of activity of the Bureau of Health of Manila in causing investigation of all cases of death with enlarged superficial lymphatic glands as one means of detecting cases of bubonic plague, several of the cases of the present series were encountered. I am also informed by workers in the Bureau of Health that several cases were encountered clinically with enlarged femoral or inguinal glands in which there was a brief period of hyperpyrexia of unexplained origin, the enlargement of the glands persisting after the subsidence of the fever. Such cases were sometimes referred to as cases of "glandular fever," and it seems not impossible that some of these cases may come within the category under consideration. This seems more probable in view of the recognized susceptibility of individuals of the lymphatic constitution to slight infections.

From another standpoint, the recognition of the lymphatic constitution is of importance among Filipinos; that is, on account

of the similarity of some of the clinical and pathological manifestations of status lymphaticus and those of beriberi. In a well-developed case of beriberi with neuritis, œdema, and gastric and cardiac disturbances, there is no danger of confusion of the two diseases. But in cases of sudden death where clinical observations have been meager or not made at all, both conditions should be borne in mind. Their occasional similarity, coupled with the extreme frequence of the diagnosis of beriberi and the complete absence of that of status lymphaticus in the records of the statistical division of the Bureau of Health, would seem to make it very probable that some cases of status lymphaticus have been classified as cases of beriberi. The clinical symptoms of infantile beriberi recently described by Andrews(16) of this department are frequently those which have been recognized as characteristic of status lymphaticus, and the appearance of the child is practically the same. This is especially true of those cases referred to by Andrews as those of the acute pernicious type of infantile beriberi. The anatomical findings in the two diseases are frequently very similar, the degeneration of the nerves which can only be recognized by appropriate microscopic technique being the only characteristic of infantile beriberi which has not been found in cases of status lymphaticus. The possibility of the association of the two conditions should be recognized.

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ILLUSTRATIONS

PLATE I

Lower end of ileum showing hyperplasia of solitary follicles and Peyer's patches in status lymphaticus. (Drawing by Castro.)

PLATE II

Organs of the neck showing hyperplasia of faucial and lingual tonsils and lymphoid tissue in the pyriform fossæ in case 2. (Photograph by Cortes.)

PLATE I. HYPERPLASIA OF LYMPHOID TISSUE OF ILEUM IN STATUS LYMPHATICUS.

PLATE II. HYPERPLASIA OF LYMPHOID TISSUE OF PHARYNGEAL RING IN STATUS LYMPHATICUS.

PRIMARY SARCOMA OF THE SMALL INTESTINE[1]

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Within the last year three cases of primary sarcoma of the small intestine have been encountered in the service of this department. In view of the infrequency of this condition, these cases have been summarized and are here presented, together with a brief consideration of the pathological anatomy of the disease.

CASE 1. (S. P. 654.)—The patient was a male Filipino, aged 33, a cigar maker. For four years he had had abdominal pain after eating, which could be relieved by induced vomiting, and the bowel movements had been irregular. In spite of symptoms of obstructions, he was fairly well nourished. A movable tumor was felt in the abdomen. The tumor was removed at operation, and the patient was in good condition three months later, after which he was lost sight of.

Description of tumor.—The available records do not state exactly which part of the intestine was removed.

A segment of the small intestine, 10 centimeters in length, was completely encircled, and the wall diffusely infiltrated by the tumor. In the distal portion of the segment, where the wall measured 1 centimeter in thickness, the lumen was markedly narrowed, while above it was dilated and the wall thinner. There was no ulceration, the mucous surface being smooth and without folds. Enlarged lymphatic glands were found in the mesentery.

Microscopic examination.—A section through the infiltrated intestinal wall showed partial absence of the epithelium, but the denuded portions showed no necrosis or evidence of ulceration. The various coats of the intestine could not be differentiated since the entire wall was infiltrated by tumor cells. The cells were round, slightly larger than lymphocytes, and had pale-

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staining nuclei and a small amount of cytoplasm. They were for the most part fairly uniform in size and shape, although occasionally large forms were seen. Connective-tissue fibers and cells and blood vessels were numerous. Here and there were bundles of muscle fibers, many of which were swollen and evidently degenerated. Where the epithelium was present, the tumor cells extended up to it, and the glands were few and short, and the villi absent. *Diagnosis:* Lymphosarcoma.

CASE 2. (NECROPSY, 1777.)—The tumor occurred in a male Filipino, aged 31, a sailor. The first symptoms occurred about three months before death when he began to have paroxysmal attacks of pain in the right hypochondrium, followed about a week later by jaundice which soon disappeared. When admitted to the hospital two months after the beginning of the symptoms, the patient was emaciated, and a soft tumor, the size of an orange, could be palpated below the right costal margin. Laparotomy was performed three weeks before death, but the condition was found inoperable.

Necropsy findings.—In the right hypochondriac region were numerous fibrous adhesions binding the liver to the diaphragm and the pyloric portion of the stomach to the liver. Behind the transverse colon lay the greatly enlarged duodenum. The stomach and upper part of the small intestine contained a large amount of blood. The pylorus was large, and opened into a greatly dilated duodenum. This dilated portion measured 16 centimeters in length, ending at the beginning of the transverse portion of the duodenum, and its lumen measured 20 centimeters in circumference at the widest part. The mucosa was destroyed in practically all of this dilated portion, the surface roughened and fissured, and from the posterior wall small irregular yellow and reddish black necrotic masses projected. The wall of the cavity was thickest posteriorly, and was everywhere thicker than the normal intestinal wall. The papilla of the common bile duct, with the pancreatic duct opening into it, was found 11 centimeters from the beginning of the dilation. The mucosa of the lower 2 or 3 centimeters of the common duct was thickened and slightly roughened, but proximal to this was normal. The growth had invaded the upper portion of the head of the pancreas, giving to it a moist homogeneous appearance. The lymphatic glands behind the duodenum were much enlarged, and some were almost entirely necrotic. Ten centimeters below the dilation was a small plaque projecting into the intestine over which the mucosa was intact. In the upper part of the ileum were found 3

small infiltrative growths, the largest completely encircling the intestine and measuring 5 centimeters in length and 5 to 7 millimeters in thickness. This appeared as a grayish patch from both the mucous and the serous surfaces, and projected slightly into the lumen, but did not diminish it appreciably. The folds of the mucosa were partly obliterated, but there was no ulceration. The other two growths nearby had the same general appearance, but were not completely circular. The mesenteric glands opposite all of these were enlarged and firm. There were no metastases to other organs.

Microscopic examination.—The tumor was very cellular, the cells showing great variations in size although the majority were slightly larger than small lymphocytes, round, with pale-staining nuclei and scanty cytoplasm. Multinuclear cells, which seemed to occur in groups, and mitotic figures were not infrequent. In the duodenum the intestinal wall was made up practically of tumor tissue and the inner surface was largely necrotic. Examination of one of the tumors in the ileum showed that growth had occurred in the submucosa and mucosa, while the muscular coats were not invaded. The infiltration extended between the crypts, which were rather few, to the surface, which was covered only partially by epithelium and showed occasional small necrotic areas. The tumor cells of this section were more typically lymphoid, and the multinuclear cells were infrequent. Mallory's aniline blue stain revealed a delicate connective-tissue reticulum throughout the tumor tissue. The enlarged mesenteric and retroperitoneal lymphatic glands showed the same general structure with frequent necrosis. *Diagnosis:* Lymphosarcoma.

CASE 3.[3] (NECROPSY, 1963.)—The patient was a male Filipino, aged 27, a soldier. The first symptom was an attack of abdominal pain on June 7, 1912, which kept him from duty for three days. On June 23, an abdominal mass was noticed. At this time, on account of rapid loss of weight, he was sent to Manila for hospital treatment. On July 10, a laparotomy was performed and an inoperable tumor was found. The patient died August 10, 1912.

Necropsy findings.—The body was greatly emaciated. The tumor occurred in the ileum, 1.5 meters from the ileocæcal valve. It almost completely encircled the intestine lying within its walls and extending for 2 or 3 centimeters between the layers of the mesentery. Its longitudinal diameter was about 8 centimeters.

[3] I am indebted to Maj. S. C. Gurney, medical division, Philippine Constabulary, for the clinical notes on this case.

At the point of greatest infiltration, the intestinal wall was about 1 centimeter in thickness. The lumen of the intestine was not encroached upon but rather enlarged. There were one or two small erosions of the mucosa, and at the thickest portion of the tumor was found a deep ulcer 3 centimeters in diameter with smooth, sloping walls.

The mesenteric glands were large, firm, and pale, and about them was often found a diffuse infiltration of the mesentery and of the retroperitoneal tissues. The retroperitoneal glands were also enlarged and some were softened. On the anterior surface of the right ventricle of the heart was a small, pale, circular nodule, slightly elevated, measuring about 0.5 centimeter in diameter. There were no metastases in other organs.

Microscopic examination.—Sections from the thickest part of the intestine showed the tumor to be made up of small groups of cells of lymphoid type, between which were coarse bands of connective tissue, often hyaline, and numerous cells which were evidently of inflammatory origin. In the younger metastatic tumors of the lymphatic glands, the connective tissue and adventitious cells were much less prominent and only a fine reticulum was present. Eosinophilic cells were rather numerous, and multinuclear cells were present, but mitotic figures were rare. Blood vessels were numerous, especially in the metastatic growths.

The nodule in the heart consisted of a small area not definitely circumscribed, showing diffuse infiltration of the muscle by tumor cells with little change in the muscle fibers. *Diagnosis:* Lymphosarcoma.

That primary sarcoma of the intestine is infrequent is evidenced by the statistics of various pathological institutes. Thus Smoler(1) reports that among 13,036 necropsies performed at Prague, in a period of fifteen years, there were but 13 cases, of which 10 were of the small intestine. Corner and Fairbank(2) in 1904 were able to collect from the literature but 65 cases, although, according to Kaufmann,(3) Rademacher(6) reviewed 140 cases in 1908, adding one new one. In our series of 2,200 necropsies, the two given above are the only ones of undoubted primary sarcoma of the intestine. The disease may occur at any age, the youngest case reported being a congenital one and the oldest 70 years of age, although it appears that the greatest number occurs in the fourth decade. In the cases reported, the proportion of males to females has been about two to one.

The small intestine is evidently more commonly the site of origin of sarcoma than is the large intestine, since Jopson and White,(4) in 1901, could collect but 22 cases of sarcoma of the large intestine, while Libman(5) the year before had brought together 64 of the small intestine. The ileum is the portion most commonly affected.

Of the types of sarcoma found, lymphosarcoma is the most frequent, but spindle-celled, round-celled, and melano-sarcomata as well as endotheliomata occur.

The tumor most frequently occurs as a spreading, infiltrating growth, completely or nearly encircling the intestine, but may occur as a polypoid mass projecting into the lumen. The growth is usually confined to the intestinal wall, leaving the serosa intact. Ulceration, on the other hand, is frequent and may cause perforation. It is remarkable, however, that very extensive infiltration of the intestinal wall, including the mucosa, can take place without ulceration, as is exemplified by case 1 of this series. Dilatation is more frequent than stenosis. This is apparently due to the widespread infiltration and destruction of the muscular coats with possibly the additional factor of accumulation of intestinal contents on account of the absence of peristalsis. The annular form of the tumor, however, can cause constriction as is shown also by case 1. When complete obstruction occurs, it is most often due to intussusception.

Metastases from intestinal sarcomata occur most frequently in the abdominal lymph nodes, particularly with lymphosarcomata, but metastases in the intestine, liver, spleen, kidneys, lungs, and brain have been recorded. Involvement of other abdominal organs seems to occur most often by direct extension from the metastatic growths in the lymphatic glands.

All of the cases here presented have been lymphosarcomata, and all have exemplified the annular form, while one shows the infrequent condition of stenosis. In all there have been metastatic growths in the abdominal lymphatic glands with more or less widespread extension from these. In but one case, in which there was a small nodule in the heart, was there metastasis beyond the abdomen.

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TUMORS OF THE PITUITARY GLAND

REPORT OF A CASE OF PITUITARY GLIOMA [1]

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Two plates

The absence in the literature of reports of similar pituitary tumors justifies the publication of the present case. Weichselbaum(21) was one of the first investigators to whom we owe the description of pituitary cysts, lined with ciliated epithelium, and containing a homogeneous or granular material. Beck(3) and Weigert(22) have described several dermoid cysts of the pituitary body. The first case of neuromyoma made up of striated muscle and medullated nerve fibers was reported by Hale White.(1) Rayer,(13) Rokitansky,(16) and Langer(1) have observed several cystic tumors which it is presumed originated from the infundibular canal. The first case of lipoma is that of Weichselbaum. (21) The report of two cases of angioma and chondroma, respectively, is attributed to Lancereaux.(1) Several cases of adenoma have been encountered (Breitner,(6) Einsenlohr,(8) and Von Hippel(9)). Adami and Nicholls(1) have described an endothelioma and a perithelial angiosarcoma. Colloid carcinomata and melanosarcomata have also been reported. Soemmering and Lancereaux(1) found several cases of echinococcus cysts. Battiscombe(7) has reported an abscess. Beadless,(2) Boyce and Beadless,(5) and Weigert(22) described several caseating tumors; and the description of syphilomata belongs to Lancereaux.(1)

The above facts prove the absence of reports of pituitary gliomata in the literature, none of the authors cited having reported such a pituitary neoplasm.

Of the 2,000 autopsies performed in the city, San Lazaro, and Bilibid morgues during five consecutive years, there is no analogous case.

[1] Read before the Ninth Annual Meeting of the Philippine Islands Medical Association, held in Manila from November 4–7, 1912.

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As an introduction, some consideration of the histology and physio-pathology of the pituitary body may be recorded.

The anatomical formation peculiar to the gland is that of a pea-shaped mass, connected to the base of the encephalon by means of a delicate peduncle. It weighs generally from 3 to 6 decigrams, and occupies a cavity in the cranial floor called the "sella turcica." It consists of an anterior and a posterior portion, together with a ramus or infundibulum. The anterior or glandular portion consists of a stroma of connective tissue, rich in capillaries, in which are closely packed epithelial cells grouped in the form of acini. The cells which constitute these acini are polyhedral, round, or oval, and are of two principal varieties, chromophilic and chromophobic. In the chromophilic cells the cytoplasm is abundant and contains granules which are stained red or yellow with eosin or take a purple coloration with hæmatoxylin. Klotz(1) has remarked the constant presence of acidophilic, mononuclear cells. The chromophobic or principal cells are smaller, more numerous, and have a transparent protoplasm. According to Berkeley,(4) the nerve elements are derived from the sympathetic plexus of the carotid. At the periphery of the lobe and particularly at the boundary line between the two lobes, the so-called pars intermedia, the acini, surrounded by cubical cells, are often distended by a colloid substance, which is also present in the lymphatic and vascular spaces.

The posterior or infundibular portion of the gland is composed of vascular connective tissue, in which exist numerous fusiform or stellate cells which are often pigmented. The structure is practically that of the neuroglia. Berkeley(4) has reported the presence of ganglion cells and of varicose nerve fibrils, but Kölliker(1) denies the existence of nerve elements in this portion of the gland.

At the line of junction between the two lobes, the vessels are particularly numerous, and in man there is a bilobular cavity bounded by cylindrical epithelium.

Physiology.—The nature of the function of the gland, although obscure as yet, is becoming more and more clear. Evidence is accumulating which tends to prove that, like the thyroid and the suprarenals, it belongs to the group of ductless glands, and that it elaborates an internal secretion essential to metabolism. As regards its vascularity, presence of acini, and lymphatic vessels containing colloid, a close analogy exists with the thyroid, which

according to general opinion elaborates an internal secretion. Schnitzler and Ewald(18) have shown experimentally the presence of small quantities of iodine in the pituitary gland. In addition, there is an hypertrophy of the organ after thyroidectomy in animals (Rogowitch,(15) Hofmeister(1)), and in cases of thyroid atrophy in man. The abnormalities of growth and development known as acromegaly and gigantism are in the majority of cases associated with lesions of the pituitary body, such as cysts, hypertrophies, or tumors. In acromegaly it has also been found that the thyroid is sometimes atrophic or cystic, and that the disease can be complicated by myxœdema or exophthalmic goitre. Some relation seems to exist also between the pituitary gland and the genital organs. Nicholls performed an autopsy on a woman about 30 years old with a pituitary tumor, in whom the genitalia were in a marked state of infantilism; a similar phenomenon has been observed in man by Pechkranz.(12) Genital deficiency, genital hypoplasia, and malformations have been noted with frequency in acromegaly by Garnier et Santenoise,(1) Thoma,(20) and Babinsky.(1)

Through the observations of Marie(10) it has been recognized that there exists a close relationship between the abnormalities of the pituitary body and the hypertrophy of the bones of the face and extremities, a pathologic condition known as acromegaly. This condition takes place during the age of virility, and its development is slow, up to twenty or more years. There is an enlargement of the face, the superior and inferior maxillary bones being particularly affected; the ears reach a very large size; the nasal fossæ are widened; and the eyelids thickened. The hands and feet are so characteristically enlarged as to be disproportionately enormous.

In generalized gigantism one frequently observes enlargement of the pituitary body. Marie inclined to the opinion that absence of active pituitary secretion induced acromegaly with replacement of the pituitary tissue by neoplasm. Schäfer(17) to whom together with Oliver and Herring we owe our recent knowledge of the subject, believes with Tamburini and Woods Hutchinson (1) that the neoplasm is due to overdevelopment of the anterior lobe, as in some cases a simple hyperplasia of this region has been observed; Von Hansemann(1) affirms that those tumors of the anterior lobe are simple adenomata and not sarcomata, or rather colloid accumulations which are associated with the disease. Schäfer suggests that the observations of Marie, in the

cases cited by the latter, can happen on the supposition that the condition commences by simple hyperplasia, the neoplasm being the terminal phenomenon.

But if the facts indicate that this anterior glandular portion furnishes hormones or other products which stimulate the development of bone or connective tissue, the observations of Herring show that the intermediate portion, also glandular, develops colloid material which finds its way through the nervous posterior portion of the gland, which is directed toward the infundibulum, and thence to the cerebral ventricles. This internal secretion elaborated in these two portions has different but equally useful properties, which, as Howell(1) has shown, is not present in the extract obtained from the anterior portion. According to experiments carried out by Oliver and Schäfer,(1) an extract of these two portions produces a rise of blood pressure very similar to, but more prolonged than, that induced by suprarenal extract, plus an increase of urinary secretion or polyuria absolutely independent of blood pressure, but directly due to the action of the extract on the renal tissues. Similarly to adrenalin, this extract is indifferent to warmth or heat. The indications are that the gland produces not one but several hormones. Like the suprarenals this diminutive gland, which in man weighs only 0.5 gram, is essential to life, and according to the experiments of Paulesco(11) and Reford and Harvey Cushing(14) its extirpation in animals in the laboratory is followed by death within forty-eight hours or more, with marked symptoms of inanition. The essential cause of this death is yet unknown. It is, nevertheless, a significant fact that this diminutive organ, essentially glandular, should exercise such an extraordinary influence in the life of animals.

REPORT OF CASE

The condition of the patient and the impossibility of obtaining a history made it impossible to get many clinical facts about the case. The post-mortem examination showed a case of simple pituitary lesion, that is, one without the accompaniment of acromegaly.

Clinical history.—It was an emergency case. The patient was found in the street in an unconscious state.

Personal data.—The patient was a male, name, age, and occupation unknown. However, his age must have been between 30 and 35 years. Family antecedents and social position were unobtainable.

Actual condition of the subject.—When first seen, the patient was in bed with dyspnœa and general convulsions. The pulse was small, slow, and thready; no fever; hypothermia was present; there was no paralysis. He was of strong frame and well nourished; his development was normal. It was impossible to obtain further symptomatological facts than those

noted, owing to the unconscious state of the patient and the absence of relatives or friends capable of supplying them.

Observations.—Five hours after admission. The patient has remained comatose since admission, in spite of the treatment instituted. A few moments afterwards the convulsions lessened gradually, and a general progressive adynamia declared itself.

The cadaver was brought to the city morgue with diagnosis undetermined. The following is the report of the autopsy performed seventeen hours after death, with histological examination of the affected viscera.

The cadaver is that of an individual of good musculature, corpulent, of medium height (163 centimeters), with a weight of 53.6 kilograms. There is cadaveric rigidity present in both superior and inferior extremities and lividity in the dependent parts. Some eschars are present on the body. There is a tattoo with initials L. R. on the anterior surface of the left forearm. No enlargement of the superficial lymphatic glands can be detected. Pupils are slightly dilated; face normal; thorax well shaped; abdomen plane. Genitalia are well developed without apparent solution of continuity, recent or remote. No evidences of hypertrophy of the osseous system are present.

The subcutaneous adipose tissue is in normal quantity, and has a dull yellow color. The muscular tissue is perfectly developed. The tissues have a normal appearance.

The peritoneum is smooth and glistening. There is a normal quantity of peritoneal fluid. The appendix and intestines are normal. The omentum covers the guts like an apron, and is 3 centimeters below the umbilicus. The liver is not prolapsed. There are adhesions between the anterior surface of the liver and the abdominal surface of the diaphragm. This latter rises to the level of the fourth interspace on the right side and to the level of the fourth rib on the left.

The *pericardium* is smooth, whitish blue, and contains approximately 5 cubic centimeters of an orange-yellow liquid. The *heart* is soft, and normal in size; it contains post-mortem coagula; the musculature is firm, normal in aspect; the valves are fine and elastic. The aorta is normal except at the base where there is a slightly raised area, which is translucent, fibrous, and 6 millimeters at its widest diameter.

Lungs.—The lungs are adherent to the thoracic and diaphragmatic walls. They are crepitant except in certain spots. The surface is somewhat rough, due to adhesions at the apex of the superior and base of the inferior lobes, and is dark gray anteriorly and reddish posteriorly. Several nodular indurated areas are felt on palpation. Section across these indurated areas shows congested collections of tissue from 5 to 15 millimeters in diameter situated, apparently, about the bronchial terminations, and slightly raised from the pulmonary parenchyma. Scraping the surface loosens some fibrin filaments from the bronchial infundibula, together with a serosanguineous exudate from the air vesicles.

The bronchi are slightly congested, and contain frothy exudate. Microscopically, there is a dense infiltration of red and white cells around the bronchioles. The epithelial lining of the bronchi is detached in part from its basement membrane, and the cells occupy the lumen of the bronchi, together with a fibrinous exudate in the form of a network in whose meshes are red blood-cells and leucocytes. The air vesicles, vessels, and lymphatic spaces are loaded with red globules.

Spleen.—It is adherent to the diaphragm and to the abdominal wall. The splenic substance is firm, and on section shows a reddish pulp with a few grayish spots. The Malpighian corpuscles are well defined, as also are the trabeculæ.

Kidneys.—These are relatively small. The capsule strips with some difficulty, tearing in places and leaving a slightly rough surface, with a few retention cysts wedged in the renal substance. Section shows a cortex 5 millimeters thick, with a pale gray color in which one can distinguish the striæ with difficulty, the glomeruli remaining completely invisible. Fœtal lobulations still persist. Microscopically there is a moderate hyperplasia of the intertubular connective tissue. The epithelium in many uriniferous tubules is loose and lying in the lumen. There is proliferation of round cells around the glomeruli and in the intertubular spaces.

Suprarenal capsules.—These are about normal in size. The cortex is thin and has a pale yellow tint with yellow areas scattered in the surface, and encloses a small quantity of milky white medulla.

Liver.—This organ is adherent to the diaphragm and high-toned in color, of firm consistence, and has a sharp border. Section shows a congested surface with clearly defined lobulations. Microscopically there is a rather extensive extravasation of blood between and over the hepatic cells. The central and interlobular veins are distended by the presence of red globules.

Gall bladder.—It is adherent to the under surface of the right lobe of the liver. It contains sirupy, greenish yellow bile. The walls of the viscus are slightly hypertrophied. The biliary tract is free.

Stomach.—It contains a dark red, viscid fluid mixed with the rugosities. There is slight hyperplasia of the lymphoid tissue.

Duodenum.—This organ is normal.

Pancreas.—It is of firm consistence. Section shows grayish lobulations, spotted with a bloody tint. The duct of Wirsung is free.

Intestines.—These are normal with the exception of the presence of a few ascarides. The mesenteric nodules are palpable, but not swollen.

Organs of the throat.—These are normal excepting a slight hyperæmia of the trachea. The *thyroid gland* is not markedly hypertrophied, but is slightly more bulky than normal. The *thymus* is atrophied and fatty.

Cerebrum.—This shows at its base an encapsulated bilobar tumor involving the pituitary body and its infundibulum. The capsule isolates it completely from the cerebral substance, and internally it is slightly adherent to the neoplasmic contents. The two lobes of the tumor are joined one to the other, the anterior lobe being larger than the posterior. The former has a more or less spherical form with a diameter of 8 centimeters, lies between the pons varolii and the olfactory bulbs in the anteroposterior axis, and extends over the internal surface of the temporal lobes in the transverse axis. The second or smaller lobe is 3 centimeters in diameter, and is the portion of the tumor which, circumscribed by the circle of Willis, is lodged in the sella turcica. It is somewhat firm and of a clearer color than the larger lobe. Over the surface of both lobes there are various nodular growths more or less of the size of a pea. The tumor on the whole is soft, fluctuating, and can be entirely enucleated from the cranial floor. The surrounding cerebral substance is softer and more friable than normal. The contents of the tumor is soft, semiliquid, dark, and seems to be a voluminous hæmatoma with

grayish bands which cross through the mass in different directions. By the side of the tumor passes the optic nerve which is more or less compressed as well as the left olfactory bulb, and probably also the optic chiasm. The third or oculomotor nerve appears to be intact. The base of the encephalon is considerably compressed by the larger lobe of the tumor, above which there is a well pronounced depression in the cerebral substance. Also the base of the left frontal lobe appears so flattened from behind forward that its anteroposterior diameter has been reduced to half its normal size. The same compression is exercised over the temporal lobes, increasing the distance between the two.

The cranium with the exception of a few small cavities, irregularly marginated, in the enlarged sella turcica, does not show any other anomaly of importance.

Microscopical examination of the tumor.—The tissue was fixed and stained by the method of Mallory for the neuroglia (phosphotungstic acid and hæmatoxylin stain) and by the ordinary procedures of staining with eosin and hæmatoxylin.

On the surface of the section there is a band of fibrous connective tissue which represents the capsule. Immediately within this there is a zone of cells, more or less closely packed, with round bluish nuclei and a moderate quantity of protoplasm which possesses a certain affinity for eosin, with outline more polygonal than circular, although there are some few of the latter type. Interposed between these cells are some rather pale-red globules. Sometimes these cells group themselves around spaces more or less oval, simulating blood vessels loaded with red globules. Some fusiform, long, delicate cells are insinuated between the groups of cells.

The subjacent zone is composed of cells of almost the same size as the preceding, with round nuclei, less dark, and with a small quantity of transparent protoplasm, in whose periphery are projections of radiating apophyses which give to the cell a stellate shape. These appendices appear to be connected with one another, but there are some free and isolated. One can find, irregularly distributed, some spaces more or less irregular, without a definite wall, and surrounded by one or two rows, often interrupted, of cubical cells so similar to the stellate cells in size that it is difficult to establish an exact distinction owing to the close packing of the former. Within these spaces there seems to be some homogeneous rosy substance. Inserted between these are found spaces without evident walls, as a mechanical effect of mere separation of the cells to give access to a group of red globules which, densely packed in the cavity, spread themselves among the stellate cells of the periphery.

The innermost or deepest zone offers a more remarkable aspect. Islets are seen, generally connected with one another, isolated occasionally, made up entirely of stellate cells identical with those of the anterior zone; between these islets there are spaces which, insinuating themselves between the cell masses, distribute the blood to all parts of the zone. These extensive spaces lack walls, and their borders are simply limited by the peripheral cells of the islets. Within the latter there are leucocytes, probably of a migratory character as they are few in number.

Scattered between the last two zones are found stellate cells disposed around a more or less oval space, apparently without lining, but examin-

ing more closely one can distinguish a subtle thread of fibrous connective tissue describing a circle or ellipse outside which the cells are disposed in irregular rows, but perpendicular to the circumference. These spaces are generally free.

DIAGNOSIS

The complete isolation of the tumor-mass from the brain-substance, its occurrence in the pituitary region, the visible destruction of the pituitary gland by the overgrowth, its hæmatoma-like appearance, the extensive proliferation of the stellate cells or glial cells, the presence of acinus-like disposition with a material very much like colloid contained in their lumina, the occurrence of widespread hæmorrhage owing to its vascularity with possible formation of new blood vessels, and lastly the lack of evidence of metastasis anywhere in the body are facts that point undoubtedly to a diagnosis of *telangiectatic glioma of the pituitary body.*

EFFECT OF THE TUMOR ON THE CIRCULATION

The tumor was treated in the following manner: Pieces cut from the two lobes of the tumor were inserted in a flask and placed in running water to displace the formalin; after sixteen hours they were removed and pulverized in a mortar. To the powder thus obtained, its estimated weight being 5 grams, were added 30 cubic centimeters of normal saline solution. The mixture was then filtered, and the filtrate used for the injection. The carotid artery was used for taking the blood pressure, and intratracheal respiration was used for the respiratory curve.

Two cubic centimeters of the filtrate were injected into the circulation of a dog, and the effect was a rapid fall of the blood pressure. Schäfer and Herring(1) found that watery extracts of the intermediate and nervous portions of the normal pituitary body produced antagonistic effects on the blood vessels. They assert that in the first injections a vasoconstrictor action predominates while in the subsequent ones a depressor action prevails. From these facts, it is justifiable to suppose that the vasoconstrictor action of the pituitary body in the present case was totally destroyed by the tumor, only the active depressor principle remaining, or that both active principles were eliminated during the process of replacement of the pituitary tissue by the neoplasm, and that the depressor effect of the emulsion was due to decomposition, or that, at least, the vasoconstrictor principle had been dissolved in the formalin in which the specimen was preserved. That this latter is possible is demonstrated by the fact pointed out by Suzuki(19) that formalin dissolves or draws out the vasoconstrictor bodies in the suprarenal glands. In default, therefore, of a true biological explanation of the phenomenon, it is as well to point out here those three possibilities.

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Case 2. *A Cellular Growth in the Infundibulum.*
Case 3. *Enlargement of Hypophysis Cerebri.*
Case 4. *Cyst of Hypophysis Cerebri.*
Case 5. *Cystic tumor of Hypophysis Cerebri.*
Case 6. *Case of Acromegaly with Cystic Hypophysis Cerebri.*
Case 7. *Tumor of Hypophysis Cerebri (probably secondary).*
Case 8. *Cystic tumor of Hypophysis (probably dermoid).*
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ILLUSTRATIONS

(Colored drawing by Castro; photographs by Cortes)

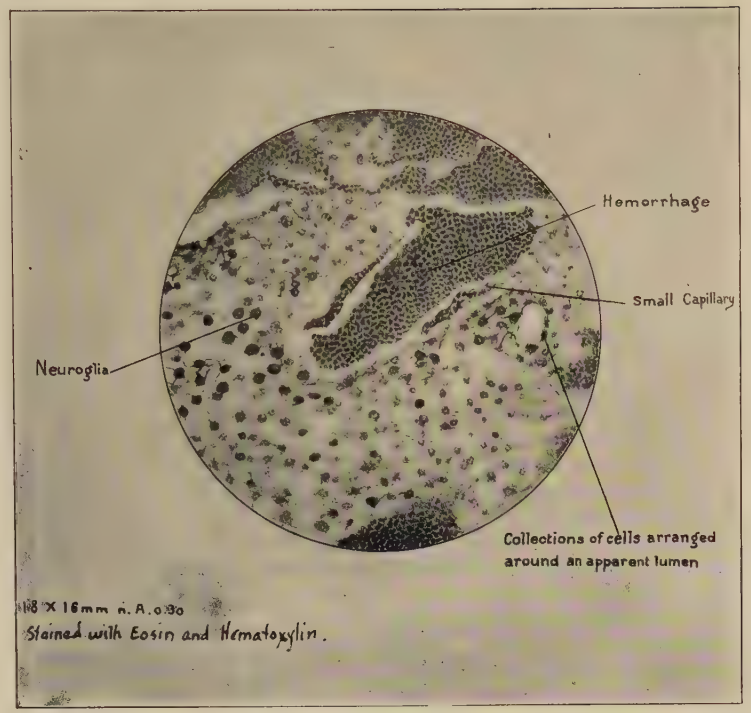
PLATE I

FIG. 1. Photograph from colored drawings of microscopical section of the hypophysial tumor.

2. Same as above.

PLATE II

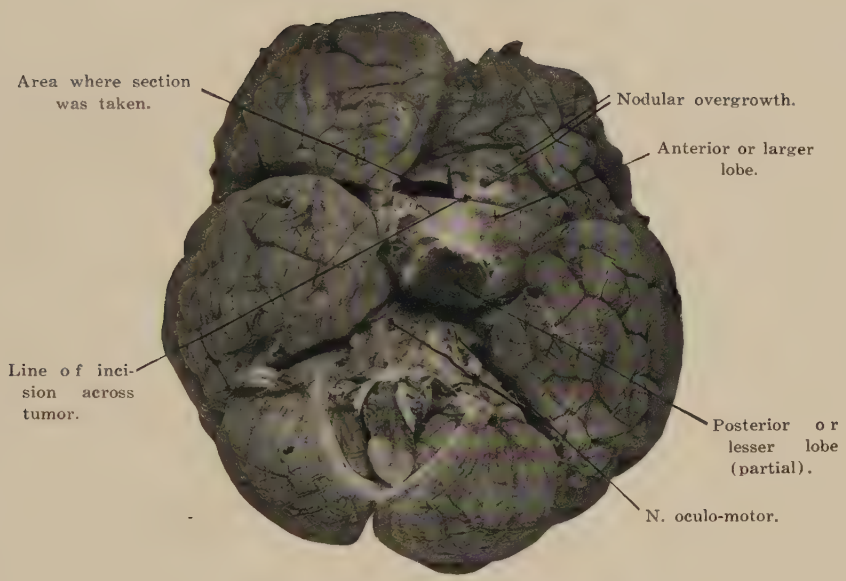
Pituitary telangiectatic glioma.



Capsule
New capillaries
Large space lined with glia and filled with blood
Glial cells
Free spaces lined with glia
Islets of glial cells
Irregular spaces loaded with blood without evident lining.
6 x 16 mm n.A.0.30
(Stained with Eosin and Hematoxylin)

Figs. 1 and 2. Microscopical section of the hypophysial tumor.

PLATE I.



PLATE, II. PITUITARY TELANGIECTATIC GLIOMA.

THE OUTBREAK OF PLAGUE IN MANILA DURING 1912

THE INSIDIOUS BEGINNING, WITH A DISCUSSION OF PROBABLE FACTORS CONCERNED IN ITS INTRODUCTION [1]

By VICTOR G. HEISER [2]

(*From the Bureau of Health, Manila, P. I.*)

One map

After an absence of six years in human beings, and five years among rats, plague was again found in the Philippine Islands on June 19, 1912. On account of the almost daily communication which Manila has with badly plague-infected foreign ports which are within a few days' steaming distance for the average vessel, and since, therefore, passengers, crews, rodents, and vermin may arrive well within the incubation period of the disease, it seems remarkable that the Philippines should have remained free from plague for so many years. During this period, plague has been detected from time to time, among human beings upon incoming vessels, but such infections were invariably intercepted at quarantine. All vessels plying between the Philippines and Oriental ports have been fumigated with sulphur, at not greater than six-month intervals, to destroy rodents and vermin.

In view of the fact that we are still in the midst of the outbreak, this paper will be confined strictly to a statement of fact, as it is not believed to be advisable, at this time, to attempt to draw any conclusions.

CHARACTER OF PLAGUE AT QUARANTINE

A most insidious form of plague was encountered at Manila last spring. On April 6, a death was reported on the steamer *Zafiro* which had arrived the day previous from Hongkong, and

[1] Read before the Ninth Annual Meeting of the Philippine Islands Medical Association, held in Manila from November 4–7, 1912.

[2] Passed assistant surgeon, United States Public Health and Marine-Hospital Service; Director of Health for the Philippine Islands; and professor of hygiene, College of Medicine and Surgery, University of the Philippines.

had, therefore, been in the harbor, at the time of the death, for a period of twenty-four hours. At the medical inspection of the vessel made at the time of its arrival, no illness was detected. The investigation showed that the victim had been on deck on the night of April 5, apparently in good health. The next morning, at 6 o'clock, he was found dead in his bunk. The necropsy and subsequent biological findings showed that death had been due to pneumonic plague. On April 7, the steamer *Loongsang* arrived in Manila from Hongkong, and the captain reported that a death had occurred the day previous in a Chinese member of the crew. Upon an investigation of this case, the captain stated that the man was, apparently, in good health, but that while hauling on a rope he fell over in an apparent faint, was placed in a chair, and in the course of a few hours was dead. The necropsy and animal inoculation showed that he had died of pneumonic plague. From this time forward, the temperatures of all the crews and passengers on incoming vessels were taken as a further safeguard.

On the arrival of the steamer *Taisang* at the Mariveles Quarantine Station, about 6.30 a. m., April 30, 1912, the entire personnel was carefully examined and found free from sickness of a suspicious nature, nor were there any elevations of temperature. Seventy-three persons were detained. At the afternoon inspection, a passenger, Co Sing, aged 51 years, Chinese, was found to have a temperature of 39° C. and pulse of 100. He was immediately placed in the hospital, but protested vehemently that he was not sick. The man was carefully watched from the first. There was a slight cough; physical examination of the chest revealed only a few râles. Smears made of the sputum and stained for plague were negative. On the fifth day the fever still continued, but the patient still insisted that he was not ill, and demanded to be released from the hospital. On this day the expectoration was blood-stained, but no suspicious organisms were noted in the smears, nor could any physical signs of pneumonia be detected. No enlarged glands could be palpated anywhere. On the morning of the seventh day the temperature and pulse dropped, and the general condition was distinctly worse. The patient now admitted that he felt ill. Several hours later the patient flinched when pressure was made in the right axilla, and slight lymphatic enlargement was made out. By the evening of this day the bubo in the axilla had increased markedly in size, the outlines of the swelling being, approximately, 3 by 7 centimeters. Glands now became palpable in other portions of the body, particularly those in the cervical

region. There were both inguinal and femoral buboes. The condition of the patient became rapidly worse, and he died at 7 o'clock on the morning of the eighth day of his illness.

At necropsy, the glands of the right axilla and those of the right side of the neck were found considerably enlarged, and the lymphatic system generally showed enlargements. There was consolidation of the lower lobe of the right lung; the spleen was about twice the normal size. In general, the necropsy findings of a typical case of septicæmic plague weré present. Smears made from the spleen and right axillary glands showed enormous numbers of typical bipolar-staining organisms. Cultures and fresh pieces of tissue, after animal inoculation had been made therefrom, were reported upon by the Bureau of Science as positive for plague.

HUMAN PLAGUE IN MANILA

On June 19, a Filipino employed as a watchman at 236 Calle San Jacinto, which is in the Chinese district, and who resided at 920 Calle Antonio Rivera, was found dead at his home, after an illness of about three days. On post-mortem examination, typical plague buboes were found in the right groin and axilla. Smears made from the spleen showed Gram-negative, bipolar-staining organisms, and inoculations made into guinea pigs resulted in typical attacks of plague. Rat catchings have been made regularly, at weekly intervals, in Manila, since the last cases of plague among rats, in 1906, and dead rats in which the cause of death was not obvious were sent to the laboratory, but no plague rats had been found since that time. The victim was a permanent resident of Manila, and had not been away from the city in many months. He lived far from the water front, did not associate with persons who had been out of the city, and since, so far as known, the nearest focus of the disease was Hongkong, the source of this infection is most difficult to explain.

The next case occurred on June 26 in a Filipina woman who lived at 1615 Calle Azcarraga, near the Arranque market. She was found alive, having been ill for three days, and, at the time she was transferred to the San Lazaro Plague Hospital, had a temperature of 41° C., and was in a moribund condition. The necropsy showed slightly enlarged glands of the left groin, but the other usual necropsy findings of plague were conspicuous by their absence. Smear preparations made from the glands of the groin and from sections of the spleen showed Gram-negative bipolar-staining organisms, and the subsequent biological exami-

nation proved positive for plague. The next case of plague did not occur until August 4—thirty-nine days later. This victim of the disease resided at 139 Calle Villalobos, in Quiapo. The case was followed by another, on August 8, at 129 Calle Villalobos (five houses removed from the former case), and by a third case, on August 21, at 352 Calle Echague. This address is just around the corner from where the Calle Villalobos cases resided. A noteworthy fact in connection with these three cases is that all were schoolboys, the oldest being 16 years of age. The disease then occurred at irregular intervals, there being but 3 cases in September, and, during October, to the 20th, there were 4 cases, all of which occurred on different streets, as may be seen from the accompanying map, the total of all cases to that date being 13. Then, between the dates of October 20 and October 22, 13 new cases occurred, so that, in a period of two days, there were as many cases as there had been during the four previous months.

EXPLOSIVE HUMAN OUTBREAK

An investigation of the large number of cases that occurred within the two days mentioned soon showed that they were all confined to laborers who worked at the Manila and Dagupan Railroad freight station. Large numbers of rats had been seen dying in, first, the north warehouse, and, a few weeks later, in the south warehouse. About three weeks after the heavy rat mortality was noticed in the north warehouse, plague appeared among the laborers in the south warehouse. It is believed reasonable to infer that the large number of cases of plague among these laborers is due to the fact that as the rat mortality was rapidly eliminating the normal supply of nourishment for the fleas, the latter began to attack human beings. This outbreak was brought to a speedy close by eradicating the rats and sprinkling the premises with kerosene to kill the fleas. The total number of cases in Manila, to November 5, was 33, and of these 30 died.

PLAGUE AMONG RATS

As soon as the first case of plague was discovered among human beings, an active rat-catching campaign was begun, efforts being concentrated to the vicinities in which human cases had occurred. Rats were caught at the rate of approximately 3,000 per month, but it was not until August 31 that a plague rat was found. This was caught in a spring trap at 351

Calle San Sebastian, which is in the same block in which the human cases on Calle Villalobos occurred. On September 7, a plague rat was found at 104 Calle Santa Rosa, and another at 215 Calle Echague, both of which addresses are within a block of the cases that had occurred on Calle Villalobos. On October 4, a plague rat was found at 644 Calle Ilaya, and another at 637 Avenida Rizal. Up to October 1 the percentage of infected rats found has been 0.005, which is unusually low, 2 per cent being considered a low average where human cases are occurring. At Hongkong, for instance, 7 per cent of the rats examined have proved to be plague-infected.

During the early part of October the rat-catching efforts were increased, and rats were being caught at the rate of approximately 9,000 per month. Other plague-infected rats were found, on October 16, at 520 Calle Jaboneros, 417 Calle Principe, and 614 Calle Salcedo; and on October 17, at 323 Calle Barcelona and 1057 Calle Padre Chavez. It is interesting to note that human cases were also found near all of these addresses.

SANITARY MEASURES EMPLOYED

Wherever a case of human or rat plague was encountered, the premises were immediately and thoroughly sprinkled with kerosene, and then disinfected in the usual way with some form of emulsion of a coal-tar product. The blocks surrounding the infected block were regarded as an infected center, and cleaning and rat-proofing measures were instituted from the periphery of such a zone and continued toward the center. This was done with the idea of driving the rats to the infected block and gradually eliminating them, and thus guarding against the spread of the infection throughout the city. For an infected center of this kind, approximately 75 laborers were employed whose duty it was to remove all accumulations of garbage and rubbish, and particularly to move wood piles, goods in warehouses, boxes, and other things among which rats might hide, and then to spray with kerosene. For the purpose of catching rats that attempted to escape during such operations, fox terriers were used with considerable success. In this outbreak, the experience had with former outbreaks, that is, that wood piles are great harboring places for rats, was repeated.

All householders in an infected zone were required to provide themselves with metal garbage cans at least 30 centimeters in height, with tight-fitting covers. The height was insisted upon particularly, in order to prevent dogs and cats from upsetting

ILLUSTRATION

Map of Manila, showing districts where plague cases occurred. 117

MAP OF MANILA, SHOWING DISTRICTS

AGUE CASES OCCURRED.

THE PLAGUE OUTBREAK IN ILOILO [1]

By CARROLL FOX [2]

(*From the Bureau of Health, Manila, P. I.*)

One map

The outbreak of plague in Iloilo was a small circumscribed epidemic, occurring in the absence of demonstrable rat infection.

A campaign against the disease was inaugurated upon the theory that infected rats had been introduced and an epizoötic had developed among the rodents of Iloilo as a result. All the precautions usually taken under such circumstances were immediately observed, such as rat catching and poisoning, rat-proofing and the elimination of rat-breeding and rat-feeding places. In addition to this, a large amount of general sanitary work was performed, such as general cleaning up, repairs and alterations to old structures, and the vacating of unsanitary dwellings. Before the work had sufficiently advanced to expect any reduction in the number of plague cases, the disease suddenly ceased. In the meantime, no infected rats had been found nor have any been found at any time since, notwithstanding the continuance of rat catching, with laboratory examination.

Upon a study of the map of Iloilo, it will be observed that there were two distinct foci of human infection; one focus comprised of one house in the nipa district and resulting in 4 cases with 4 deaths, all Filipinos; the other focus comprised of three closely associated houses in the hard material district, and resulting in 4 cases with 4 deaths, all Chinese. These foci are shown on the map as X and Y, respectively.

At the end of July, the first case occurred in house "A" followed by a case in house "B." Then there was a case in house "C." After a short period 2 cases died the same day in

[1] Read before the Ninth Annual Meeting of the Philippine Islands Medical Association, held in Manila from November 4–7, 1912.

[2] Passed assistant surgeon, U. S. Public Health and Marine-Hospital Service; Assistant Director of Health for the Philippine Islands; associate professor of hygiene, College of Medicine and Surgery, University of the Philippines.

the same house, some distance away from either focus. Investigation showed that they had been living in house "C," having left there within the week and being sick at the time of leaving. They were unquestionably infected in house "C." Following this, there developed a case at house "D," another at house "C," and another (the last) at house "D." Eight cases in all occurred within a period of less than two months.

The occurrence of a fourth case in each focus would indicate that previous disinfections had not proved efficacious. Therefore, the entire work of disinfection was repeated with petroleum and kreso. Walls, floors, beds, and chairs were thoroughly sprayed with a view toward exterminating bedbugs. In nipa houses it is difficult to reach bedbugs lurking between the layers of nipa, and, therefore, after disinfection, house "C" was vacated and closed for a period of two months. Houses in the immediate vicinity were also treated to kill bedbugs.

Double walls and ceilings in house "D" were torn out, and special effort made to exterminate the bugs.

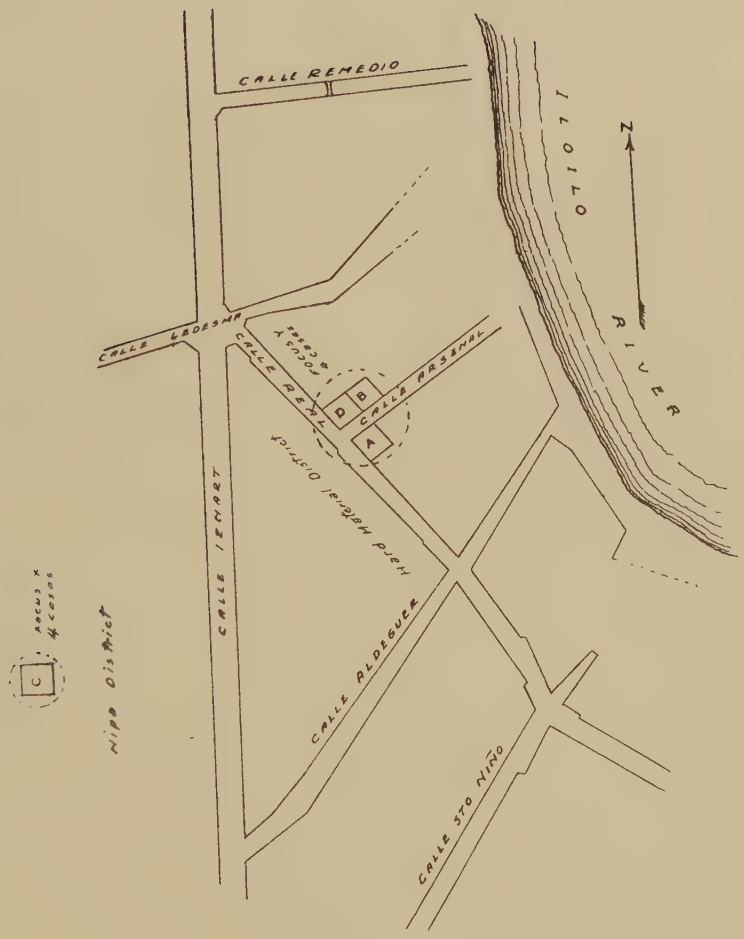
The writer is of the opinion that this outbreak of plague was an instance of bedbug transmission, starting with a case of human plague, introduced into Iloilo from Manila, where plague had previously appeared, or possibly from a plague-infected foreign port, the reasons being as follows:

1. The absence of rat infection.
2. The decidedly circumscribed foci.
3. The sudden cessation of the outbreak after the houses believed to be infected had been thoroughly treated to kill vermin.
4. House "C" was owned by a Chinaman, who was as well one of its inmates, and who undoubtedly had at least business intercourse with the Chinamen living in the focus Y, and who could have readily carried infected bedbugs from one focus to another.

It is regretted that an effort to secure bedbugs was not made earlier in the campaign so that inoculation experiments could have been carried on to prove or disprove the validity of the theory in this case. However, that bedbugs may and often do carry plague infection has been proved beyond a doubt by various observers.

ILLUSTRATION

Map, showing plague foci in Iloilo. 121



MAP SHOWING PLAGUE FOCI IN ILOILO.

Scale 1: 2,500.

SOME CARBOHYDRATE REACTIONS OF THE DYSENTERY BACILLUS [1]

By C. S. Butler [2]

(From the Laboratory of the United States Naval Hospital, Cañacao, P. I.)

Ever since the carbohydrate reactions were elected to a wider field of usefulness in bacteriology, largely through the work of Theobald Smith,(1) there have been differences of opinion among authors as to their reliability. One need only compare the fermentation tables published by different authors to note differences as regards the same organism. In some cases the same author will give different results for the same bacterium. Thus in the fourth edition (1910) of Pathogenic Bacteria and Protozoa by Park and Williams, on page 257, we find in a chart that *Bacillus dysenteriæ* (Shiga) ferments with acid production the carbohydrates dextrose, maltose, dextrin, and mannite. On page 275 of the same volume, the authors state that the dysentery bacillus produces neither acid nor gas in glucose bouillon, while on page 281 they state that the Shiga type of dysentery bacillus does not ferment mannite, maltose, nor saccharose. Here are two statements of error to one statement of fact, and while it would not bother one who was actually working with the subject, yet it does not better the general opinion of the carbohydrates as differential agents to find such opposing statements about them. Other instances of this kind could be mentioned, but it is only intended to indicate that at times the carbohydrates may not, from one reason or another, have received a fair appraisement of their real value, and it is the purpose of this paper to try and explain a few of these opposing results. As a purely theoretical proposition, it would seem logical to conclude that, if a pure culture of a given bacterium is introduced into a medium made always of the same materials and constant in reaction, with a given amount (say, 1 per cent) of a chemically pure carbohydrate added, the bac-

[1] Read before the Ninth Annual Meeting of the Philippine Islands Medical Association, held in Manila from November 4–7, 1912.

[2] Surgeon, United States Navy; and lecturer on the pathogenesis of physical agents in the Tropics, University of the Philippines.

terium should always react in a constant manner under constant conditions of time and temperature. In testing the truth of this statement, we have been led to the belief that, so far as the dysentery bacilli are concerned, the proposition is almost if not quite true, and that, so far as the practical determination of strains is concerned, it may be accepted as a fact.

Lehmann and Neumann(2) divide the dysentery bacilli into four strains according to their action upon mannite, maltose, and saccharose. The strains thus differentiated are: (1) Shiga-Kruse, (2) Flexner, (3) Strong, and (4) Bacillus Y (Hiss-Russell). The table of differentiations is as follows:

Carbohydrate.	Shiga-Kruse.	Flexner.	Strong.	Bacillus Y.
Mannite	Blue	Red	Red	Red.
Maltose	Blue	Red	Blue	Blue.
Saccharose	Blue	Blue	Red	Blue.

Other writers, basing their opinions upon the carbohydrate reactions, would differentiate them still further. It is a matter of doubt whether the group would stand further differentiation than that just indicated, provided we use pure carbohydrates and properly control our results; and most bacteriologists are content to recognize two strains of dysentery organisms; namely, those which ferment mannite and those which do not. It is generally admitted that these two types, aside from their fermentative differences, also show differences in their capacities to produce toxin and to cross-agglutinate and cross-bacteriolyse. It is doubtful whether there is any practical advantage to be derived from going further than the recognition of these two types. But it is certainly a fact that, among those which produce acid in mannite solutions, there are strains which will and others which will not ferment maltose, and there are also strains which will and others which will not ferment saccharose. These last-named saccharose fermenters seem to be very rarely isolated from dysenteric stools, and their fermentation of saccharose seems much slower and less decisive than does the action of these bacteria as a group toward other carbohydrates upon which they will act. In order to get comparable results with these reactions, it is evident that the methods employed must be comparable. It is also found that the results vary within certain limits when dealing with the same set of organisms, depending upon whether solid media or liquid media are used and also upon whether or

not the reaction of the media has had to be previously arranged. Some carbohydrates suffer inversion to a lower order if subjected to heat in the presence of weak acid or alkali, and in the finished product we will then find for instance that a supposed Shiga strain of the dysentery bacillus is producing acid in the maltose medium. As a matter of fact, it is simply showing its capacity to ferment glucose inverted from maltose. The question of the indicator is also to be considered. The one generally used is litmus, and this, if subjected to long heating in the presence of organic substances, bleaches out and we are left with a desensitized litmus. The use of litmus, too, as a part of the medium rather than as a pure indicator is a matter to criticize. What chemist would expect his indicator to show a fine shade of reaction if he incorporated that indicator into a mass of organic material, sterilized it on three successive days at 100° C., and then stored it in the ice box for perhaps a month? I have found on a number of occasions that the results varied, particularly when dealing with maltose, if the organism be allowed to grow for about three days in the peptone sugar solution, and the indicator be then run in and the results read immediately, from the results obtained by growing the same organism in the same solution, but with the litmus added from the start. If, however, the tubes, to which the indicator was added at the end of the incubation, are set aside for a few hours, they will nearly always show the same results as those to which the litmus was added in the first instance. These statements are not of much importance from the standpoint of indicating variability in the carbohydrate reactions of dysentery bacilli, because with the thousands of trials to which these organisms have been subjected by different observers I believe we are in possession of the exact facts as to what the different strains will do. But they do indicate, it seems to me, that for the individual bacteriologist, identifying strains of dysentery bacilli from the stools, the media and the methods employed should be revised and subjected to standardization. On account of our lack of standards, combined with the inherent tendency of some of our differentiating carbohydrates to change during manipulation, I believe we are overlooking at least one perfectly valid variety of *Bacillus dysenteriæ;* namely, Bacillus Y.

It is manifest that the simpler the solution into which any given carbohydrate is introduced, always provided that the bacterium will grow luxuriantly in it, the more nearly the facts will be revealed. If we could get organisms to grow in a simple

solution of the particular carbohydrate in distilled water, the reaction would be reduced to its simplest terms. But the large majority of microörganisms require proteid material in the medium, which of course introduces another factor into the equation and makes the reaction a resultant of two forces rather than the effect of one. As was intimated, the use of media for carbohydrates which require to be arranged in reaction is open to objection. It is also objectionable to use solid media for the reason that liquid media are more sensitive, and also because upon the surface of solid media where free oxygen is at hand many organisms will not ferment the carbohydrate in order to get oxygen. This latter fact is made use of in the Russell medium for identifying varieties of bacteria, but in finding out how a given organism will react toward a given carbohydrate the fluid media seem to be better. That our media should be sterile need not be emphasized. That it often is not sterile after three successive heatings for twenty minutes in the Arnold sterilizer I have found such a common experience that I have discontinued this method of sterilization of carbohydrates, and now use only the autoclave. So far, I have not found that heating for twenty minutes at 20 pounds' pressure has produced changes in any of the carbohydrates, when prepared as described below. After sterilization, the tubes are placed overnight in the incubator; such as are not sterile are discarded next morning, and the inoculations made as soon as possible. Were it not for evaporation, the 37° incubator would be a far safer place for storage of sterile media than is the ice box. It is probable that some of the varying fermentative reactions given for the dysentery bacillus have been due to contaminative organisms, and it might be added in passing that the only proper control of a "crooked fermentation" is the actual plating out and reidentification of the organism from the freshly isolated culture.

The medium which has been found to give the most constant results has been a peptone solution in distilled water—Witte's peptone, 1 per cent; the desired carbohydrate (the purest obtainable), 1 per cent; sodium chloride, chemically pure, 0.5 per cent; made up with distilled water. The medium is then distributed in test tubes, 10 cubic centimeters in a tube, and is sterilized at 20 pounds' pressure for twenty minutes. Then to each tube is added 2 cubic centimenters of a 5 per cent filtered litmus solution which has been autoclaved separately. This litmus solution is boiling at the time introduced, and the tubes are then heated in the Arnold sterilizer for fifteen minutes to ensure sterility. After

incubating overnight and culling out any infected tubes, the medium is ready for inoculation. The objections which may be offered to this medium relate to (1) the low content of carbohydrate, (2) the high temperature to which the carbohydrate is submitted, (3) the high temperature to which the litmus solution is submitted, and (4) the large amount of litmus. As to the last three objections I will only say that in my hands this method has given better results than any other. As to the first objection, that regarding the low content of carbohydrate, a few words of explanation are necessary. The effects which bacteria may produce upon carbohydrates are (1) to ferment with acid production, (2) to ferment with acid and gas production, and (3), the negative effect, to let the carbohydrate alone entirely. The intestinal bacteria and practically all rapidly growing bacteria show what they are going to do to any particular carbohydrate within five days, and most of them within forty-eight hours. This statement does not refer to slow-growing organisms such as the tubercle bacillus. With organisms which produce gas this can be shown by accurately marking off at 6-hour intervals the amount of gas in the closed arm of the fermentation tube. There comes a time within three days, provided we have not used too much carbohydrate, when the gas production stops, and if we measure at that point we shall find, at the next reading, that the fluid has risen slightly above our last mark. The organism has done all it will ever do to the carbohydrate introduced, and the medium has taken up its limit of gas at the existing temperature and pressure. If we give it more carbohydrate than it can ferment, the organism will stop growing when a certain degree of acidity is reached. Bacteria do not produce alkali from carbohydrates, but if we leave our inoculated tubes for two or three weeks in the incubator, contaminations, concentration of the medium, or the splitting of proteid may result in a change of our original picture. We are in that case, however, not reading the effect of the bacterium upon the carbohydrate, but upon some other constituent of the medium, or perhaps the effect of chemical reactions not connected with the organism at all.

In this paper space does not permit a consideration of all the qualities and peculiarities of the 8 or 10 carbohydrates with which I have worked. My attention was so soon focused upon the sources of error in the fermentation tests of the important carbohydrate, maltose, that I have not attempted to study critically the other carbohydrates from a bacteriological standpoint.

Suffice it to say that some of them will stand almost any kind of treatment without change, while some specimens of maltose sent out by our best manufacturers are already partly inverted when the packages are opened.

My plan was to study the reactions of a large number of strains of the dysentery bacillus, by running along with these a considerable number of other organisms whose exact identity was known. The same set of organisms was always planted along with the dysenteries into any given lot of medium. In this way a score of trials of the bacterial action on the several carbohydrates have been made during the past four months. Sixteen strains of *Bacillus dysenteriæ* have thus been tried a number of times against 16 other organisms under exactly similar conditions. Some of the dysentery strains were laboratory cultures for which I am indebted partly to Maj. P. M. Ashburn of the Tropical Board, and partly to Dr. M. A. Barber of the Bureau of Science. Other strains were isolated from the dysenteric stools of patients. The advantages of this method of multiple bacterial cross control will upon reflection be evident. If, for instance, as was frequently noted to be true, the 8 or 10 strains of Shiga's bacillus in the series were found to ferment maltose when they had refused to ferment mannite, it was hardly likely (with the precautions taken to guard against contamination) that all of these could be explained on the basis of mixed cultures. And, if all the other bacteria in the series acted in this set as they should have acted upon glucose, it is pretty evident that the fault lay in the maltose. If, however, an isolated tube in the series gave some unexpected result, it indicated an impure culture. That culture was then plated and reidentified. If the lactose had been hydrolysed in the manipulation, all the bacteria in the series would act not as upon lactose, but as they should act upon dextrose and galactose. If the sucrose has not remained intact, but is inverted, the baterial series will act, not as upon sucrose, but as upon dextrose and levulose. In working with the carbohydrates in this way it is soon evident that if we start with a chemically pure carbohydrate (which alone should be used in bacteriology) and do not add to it acids and alkalies, it will stand one decisive autoclaving better than it will heating for three successive days in the Arnold sterilizer. It is not requiring too much of any substance used in bacteriological work that it be able to stand the manipulations necessary to get it sterile, and, if it will not do this without change, it should be rejected. It was very soon

found that all the specimens of Kahlbaum's maltose, which we had in the laboratory, showed the fermentations characteristic of glucose, when used in fluid media. Specimens of maltose were obtained from several laboratories in Manila, and all those of Kahlbaum manufacture gave the same result, regardless of whether the sterilization was intermittent or under pressure in the autoclave. A sample of Merck's maltose was obtained from the Bureau of Science which gave the fermentative characters of uninverted maltose. Barfœd's test for monosaccharids was tried upon the Kahlbaum and the Merck maltoses, and this seemed to substantiate the idea that the Kahlbaum preparation had some glucose in it. A sample of Kahlbaum's maltose which had been in the laboratory for about one year was submitted to the Bureau of Science for analysis. The result is as follows:[3]

$(\alpha)_D$	=121.73
Water (per cent)	6.72
Corrected $(\alpha)^4$	=130°.5

Osazone test shows the presence of a small quantity of dextrose. The sample contains other impurities, some of which are insoluble.

The specific rotation of anhydrous maltose should be:

$$(\alpha)_D = 139°.2.$$

I cannot explain why Kahlbaum's preparations of maltose showed the reactions of dextrose while the one specimen of Merck's did not. The Merck's had been in the storeroom of the Bureau of Science certainly for over a year and very likely for five years. The Merck's package had not been opened, while all the specimens of Kahlbaum's except one had been opened for some time. I am inclined to explain the result, however, as due to the inherent tendency of the maltose molecule to take up water and change into two molecules of dextrose. In solid media (maltose agar) inoculated with the nonacid strain of *B. dysenteriæ*, the change is hardly manifest as the small amount of glucose present is only fermented in the depths of the stab culture, and the slight reddening is confined to the line of stab and is not manifest upon the surface. But in maltose-peptone solution, where all the glucose present is changed and where any change is reflected throughout the medium, the result is a completely red culture, whereas in a parallel tube of uninverted maltose containing the same bacterium it is entirely blue. If we grant that this tendency of maltose to invert is pretty general, and I believe that

[3] Analysis by R. R. Williams.

it is, we can easily see the effect it would have upon the determinations in this group alone. The Hiss-Russell bacillus depends upon maltose for its differentiation, and if the maltose is partly inverted this type will not be identified. An investigator using a partly inverted maltose would be led astray so far as identifying this type of dysentery bacillus is concerned, while if he tried to determine the reactions of the dysentery bacilli as a class to the three carbohydrates, glucose, mannite, and maltose, he would find his Shiga strains fermenting glucose, not fermenting mannite, but fermenting maltose. Mannite tends to preserve its identity, while maltose is unstable and tends to change. The inclination would be to explain this upon the basis of inconstancy in the fermentative action of the bacterium, whereas the cause is to be found in the impurity of the carbohydrate. Long experience has shown that the dysentery bacilli as a class ferment the three substances named above in the following order: First most readily glucose, next mannite, and third and least readily maltose. Ohno,(3) in a study of types of dysentery bacilli in 1906, found a number of organisms which, in acting upon these three carbohydrates, skipped mannite, but fermented maltose. He makes no mention of having ascertained whether or not his carbohydrates were pure. If he had his maltose partly inverted to dextrose, it would explain why many of the sera produced by his acid types agglutinated nonacid types just as well as they did the organisms used in their production.

Castellani(4) in a recent article publishes a table of cultural characters for certain intestinal bacteria, in which he states that the Shiga bacillus may or may not ferment maltose. In the same table the Hiss-Russell bacillus is put down as producing acid in maltose. Now the nonfermentation of maltose is the one differentiating character of the Hiss-Russell bacillus, and if we remove that it becomes a Flexner type. I have found in the series of organisms with which I have worked that several which were at first thought to be Flexner strains were really Hiss-Russell strains. They could be made to give the fermentations of the Flexner bacillus by simply changing from Merck's to Kahlbaum's maltose. It is believed that this instability of maltose has been generally encountered and that many of the varying results obtained by different observers may be attributed to it. If we recognize this same principle as applying also to other carbohydrates in different degrees, we can easily see that the promiscuous use of carbohydrates will, when no control is used to detect impurity or inversion, lead to wide differences in

the results obtained by different men when working with the same bacteria. In the admirable article on bacillary dysentery in Allbutt's System of Medicine, Flexner(5) states that "the number of variants among this group of bacilli is considerable, and it is probably incorrect to continue the subdivision into type indefinitely." This statement is one which we would do well to take to heart. But I believe that when the cause of the apparent variability is identified, it will not all be explained on the basis of the bacilli doing one thing one day and another the next, but rather due to the media and the methods. It would be in the interest of exact knowledge and of practical bacteriology if some scientific body or laboratory took up the question of standard methods in carbohydrate work as applied to bacteriology. During the past four months I have inoculated several thousand carbohydrate tubes with the same strains of bacteria, and in only one instance have I been unable to explain variable results by a change in the sugar or else contamination, and it is my belief that the reactions of bacteria toward pure carbohydrates are as fixed and definite as any other characters used in the identification of microörganisms.

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ISOLATION OF DIPLOCOCCUS INTRACELLULARIS MENINGITIDIS WEICHSELBAUM FROM A CASE OF CEREBROSPINAL MENINGITIS OCCURRING IN A NATIVE OF THE PHILIPPINE ISLANDS [1]

By David G. Willets and Otto Schöbl

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It has been known for several years that specific cerebrospinal meningitis is present at times in the Philippine Islands. Strong and Musgrave found 12 typical cases among American soldiers at the Division Hospital, Manila, during the winter of 1899 and 1900. Several of the patients died, and the organism was isolated at necropsy. Musgrave also isolated the organism from a Filipino who came to necropsy in 1903; this case had not been diagnosed ante mortem. We are informed that Whitmore likewise recovered it from a case of cerebrospinal meningitis, and two or three additional cases have been discovered at necropsy in the Philippines by other pathologists. One of us (Schöbl) found a Gram-negative, intracellular diplococcus in a specimen of cerebrospinal fluid sent to the Bureau of Science for examination. Cultures made from the fluid were negative and no more material was available. A Gram-negative, intracellular diplococcus was also found by one of us (Willets) in the cerebrospinal fluid of a child presenting typical symptoms of cerebrospinal meningitis; this patient came to necropsy when pronounced evidences of acute miliary tuberculosis were disclosed. It is suspected that the child had an intercurrent infection with the meningococcus. However, the cultures made from the cerebrospinal fluid obtained by lumbar puncture and at necropsy were negative for diplococci; hence the case was unsatisfactory. One of us (Willets) recently saw a child in the Batanes Islands whose previous history suggested an attack of the disease. Dr. A. G. Sison of the Philippine General Hospital has seen cases in St. Paul's Hospital, Manila, and in the Philippine General Hospital, Manila, which he believes to have been specific cerebrospinal meningitis, but the organism was not isolated either from the cerebrospinal fluid or at necropsy in any one of them.

[1] Read before the Ninth Annual Meeting of the Philippine Islands Medical Association, held in Manila from November 4–7, 1912.

Thus considerable evidence is adduced that specific cerebrospinal meningitis occurs in the Philippines. There is, however, no definite record of a case occurring in a Filipino in which the organism has been isolated and studied culturally. For this reason, it is considered to be worth while to report the findings in the present case, in order that this disease may be definitely added to the nosology of the Philippines.

Dr. Eleanor J. Pond, in whose service the case occurred, has furnished the clinical data.

Gregorio Pacheco, a 6-year-old boy of Malolos, Bulacan Province, was admitted to the Mary Johnston Hospital, Manila, on September 6, 1912, with a history of having had fever on September 2. On September 3, he had projectile vomiting. On September 4, vomiting was absent; the patient was semiconscious, and he showed some retraction of the head.

On admission to the hospital the patient was restless and somewhat delirious. Opisthotonus was marked; Kernig's sign and trismus were present; the temperature was 39°.1 C.; pulse, 125; and respiration, 33. On September 7, the restlessness was greatly increased; the body was rigid; the jaws were stiff; opisthotonus, Kernig's sign, trismus, and photophobia were present; and touching the patient produced tremors. Fifteen cubic centimeters of very turbid, cerebrospinal fluid were removed by lumbar puncture. The patient improved rapidly after this operation. On the following day, the muscles were slightly relaxed, and on the second day he was even less uncomfortable, and took milk and ice by mouth. The blood picture at this time was as follows:

Hæmoglobin	95 per cent.
Erythrocytes	4,400,000
Leucocytes	21,000
Polynuclears	74 per cent.
Small lymphocytes	15.5 per cent.
Large lymphocytes	6.0 per cent.
Transitionals	1.0 per cent.
Large mononuclears	2.0 per cent.
Eosinophiles	0.5 per cent.
Mast cells	1.0 per cent.

An urinalysis made on September 10 was as follows: yellow, acid, cloudy; specific gravity, 1.018; a trace of albumin; no sugar; ammonium urates in abundance; mucus; no pus and no casts. The temperature gradually subsiding became normal on September 11, the tenth day of the disease and the fourth day after lumbar puncture. On September 12 an offensive

ozæna, which persisted for two weeks, appeared. Blood examination made on September 13 resulted as follows:

Leucocytes	10,500
Polynuclears	64 per cent.
Small lymphocytes	20 per cent.
Large lymphocytes	5 per cent.
Transitionals	6 per cent.
Large mononuclears	2 per cent.
Eosinophiles	3 per cent.

On the following day, the urine showed a trace of albumin, otherwise nothing abnormal. On September 16 the patient sat up for fifteen minutes and asked for bread. Light was still displeasing. Fæcal examination revealed the presence of a few ova of *Ascaris, Trichuris,* and hookworm, and much mucus. On September 19 an afternoon rise of temperature to a fraction below 40° C. occurred, and the patient vomited repeatedly. During the succeeding five days there was a daily rise of temperature and headache was present. The temperature then returned to normal. On October 1 profuse perspiration was present most of the morning, and for three or four days thereafter a rise of temperature occurred once in twenty-four hours; this apparently yielded to the administration of quinine and aspirin. On October 8 the blood picture was as follows:

Hæmoglobin	95 per cent.
Erythrocytes	4,200,000
Leucocytes	13,000
Polynuclears	74 per cent.
Small lymphocytes	18.5 per cent.
Large lymphocytes	3.5 per cent.
Transitionals	2.0 per cent.
Eosinophiles	0.5 per cent.
Mast cells	1.0 per cent.

The blood was negative for malarial parasites. His appetite was poor after the rise of temperature on September 19; hence the patient became markedly emaciated. He appeared to be very homesick; therefore, his father was allowed to take him home on October 11. This change seems to have been beneficial, for his father stated on October 30 that the boy was gaining weight and walking about.

The specimen of cerebrospinal fluid was received by us on September 7, six hours after the puncture had been made by Dr. A. M. Saleeby, visiting physician at the Mary Johnston Hospital. It was very turbid, and contained numerous grayish white flakes. Smears from the sediment obtained by centri-

fuging for about twenty minutes disclosed a moderate number of biscuit-shaped, Gram-negative diplococci, which were chiefly within polynuclear cells. The polynuclears were very numerous; mononuclears, rare. Cultures on Loefler's blood serum showed a pure growth of a Gram-negative diplococcus on the following day. Subsequently, transplants were made to two tubes of each of the following culture media.

Solid media.		Liquid media.
Slants.	Stabs.	
Whole human-blood acid agar-agar.	Lactose litmus agar + 1.	Peptone + 1.
Loefler's blood serum.	Glucose agar.	Lactose bouillon.
Agar-agar + 1.		Plain bouillon + 1.
Agar-agar — 1.		
Glycerine agar-agar.		
Potato.		

In no case was the growth luxuriant. The best results were obtained with the whole human-blood acid agar-agar, while those on Loefler's blood serum ranked second. The growth on acid and alkaline agar-agar and on glycerine agar-agar was very scanty, only isolated colonies developing. Potato media gave negative results. Of the stab transplants, one of each variety gave a very slight growth along the line of puncture, and one of each resulted negatively. No growth was obtained in fluid media excepting in one peptone tube, and this was unsatisfactory since it was contaminated with staphylococci.

The isolated colonies were somewhat elevated, yellowish, moist, and rather irregular in outline, regardless of the culture medium used. As they became older, they were white and dry with serrated edges. Smears from the cultures showed the diplococci lying for the greater part in single pairs. Tetragenoid forms were not infrequent; clumps were present; but chains were absent.

The organisms behaved variously toward Loefler's methylene blue. Those from fresh cultures took the stain well as a rule, whereas those from a 48-hour culture took it poorly. Many of them were swollen in these smears, thus losing some of their biscuit shape. It was necessary to make transplants not less than once in forty-eight hours, in order to keep the culture alive.

Fermentation tests gave positive results with glucose and maltose; negative results with saccharose, lactose, and mannite.

Microscopic and macroscopic agglutination reactions were present. On September 13, the twelfth day of the disease, positive microscopic results were obtained in one hour in dilutions of 1 to 20 and 1 to 40 of the patient's whole blood. On the following day macroscopic agglutination was present in dilutions of from 1 to 6 up to 1 to 384 of the patient's blood serum, after incubating at 37° C. for two hours and allowing to stand over night.

Attempts to produce the disease in monkeys and recover the organism in pure culture were unsuccessful. The experiments were as follows:

On September 9, monkeys 6403 and 6404 were trephined. One cubic centimeter of a thin suspension of the diplococci obtained from a 28-hour culture on Loefler's blood serum was injected beneath the meninges of monkey 6403. Rather profuse bleeding rendered the operation unsatisfactory, since the meninges could not be clearly seen while the injection was being made. Monkey 6404 received 1 cubic centimeter of the 52-hour specimen of cerebrospinal fluid taken on September 7, the flakey material being avoided in so far as possible. The field of operation was clear in this case, the meninges being visible throughout the injection, and hence the operation was quite satisfactory.

During the following day the monkeys were nervous, uncomfortable, and each had a temperature of 40°C. On the second day they were greatly improved, and thereafter gradually returned to normal. No convulsions or tremors were noticed in either animal at any time after operation.

On September 17, 0.2 cubic centimeter and 1 cubic centimeter of a suspension of organisms from several 24-hour Loefler blood-serum cultures were injected into the spinal canal of monkeys 6405 and 6408, respectively.

Monkey 6408 was found dead at 7 a. m. the following morning. Necropsy was performed at 3 p. m. Smears from 4 different levels of the spinal cord showed Gram-negative, extracellular and intracellular, biscuit-shaped diplococci. Cultures from the heart's blood and the spleen were negative, while those from the four different levels of the cord gave a mixed growth of Gram-negative diplococci and staphylococci. We were unable to secure the diplococci in pure culture.

Monkey 6405 on the day after the operation was very uncomfortable, nervous, easily frightened, and found repeatedly lying upon its side. However, no tremors nor convulsions were observed. The temperature was 40° C. On September 19, approximately forty-two hours after injection, a small amount (0.2 cubic centimeter) of cerebrospinal fluid was removed by puncture; this gave Gram-negative diplococci in smears, but cultures on Loefler's blood serum were negative. The animal improved daily, and apparently returned to normal.

On September 27, 1.0 cubic centimeter, 0.6 cubic centimeter, and 0.1 cubic centimeter of a suspension of diplococci from several 24-hour Loefler blood-serum cultures were injected into the spinal canal of monkeys 6417, 6406, and 6407, respectively. On the following day all three animals were in good condition. The temperature of each was only slightly elevated. Cerebrospinal fluid obtained from each animal approximately eighteen

hours after injection was negative for diplococci. Each of the animals continued to be in good health.

Believing that the organism was becoming more and more attenuated, no further experiments were attempted. The failure to produce the disease in monkeys is attributed to the low virulence of the particular strain with which we were dealing. The clinical course of the disease in the patient lends itself to this belief.

The agglutination reactions obtained with the organism and the patient's blood, the location of the diplococcus, its presence within the polynuclear cells, its morphology, its staining properties, and its cultural characters, as herein outlined, all form a chain of evidence which, even in the absence of successful animal experiments, convinced us that it is identical with *Diplococcus intracellularis meningitidis* Weichselbaum.

While this article was in type the meningococcus was isolated by Dr. R. W. Hammack, College of Medicine and Surgery, University of the Philippines, at autopsy from a case of meningitis occurring in a Filipino 26 years of age. The organism fulfilled all of the cultural, morphological, and staining characters of *Diplococcus intracellularis meningitidis*. This is the only case from which the meningococcus has been isolated in 2,371 autopsies performed at the College of Medicine and Surgery.

THE DURATION OF PASSIVE IMMUNITY AGAINST TETANUS TOXIN [1]

By E. H. RUEDIGER

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In a previous communication [2] I reported that in guinea pigs passive immunity conferred by antitetanic serum from horse is of short duration, perhaps not longer than three weeks.

The experiments to be reported are grouped under the following three heads:

1. The duration of passive immunity in horse, after the injection of homologous antitetanic serum.

2. The duration of passive immunity in guinea pigs after an injection of antitetanic serum from horse, preceded by repeated injections of antitetanic serum from horse.

3. The duration of passive immunity in guinea pigs after an injection of antitetanic serum from horse, preceded by repeated injections of normal horse serum.

EXPERIMENT NO. 1

In September, 1911, three large, apparently healthy horses, Nos. 1, 2, and 3, were obtained for this purpose. Horse 1 received 1,500 units of antitetanic serum from horse injected subcutaneously on September 9, 1911. Horse 2 received a subcutaneous injection of 1,500 units of antitetanic serum from horse on October 9, 1911. Horse 3 was used as control.

On October 23, 1911, two weeks after horse 2 had received the serum and six weeks after horse 1 had been inoculated with serum, each of the three horses was inoculated subcutaneously with about 50 standard doses of test toxin.

TABLE I.

No. of animal.	Antitetanic serum units.	Date.	Tetanus toxin test doses.	Date.	Weeks after serum.	Result.	Date.
1	1,500	Sept. 11, 1911	50	Oct. 23, 1911	6	Lived	
2	1,500	Oct. 11, 1911	50	do	2	Lived	
3	none		50	do		Died	Oct. 30, 1911

[1] Read before the Ninth Annual Meeting of the Philippine Islands Medical Association, held in Manila from November 4–7, 1912.

[2] *Bull. Manila Med. Soc.* (1911), 3, 98.

Table I shows the results obtained. Horse 1 tolerated 50 standard test doses of tetanus toxin six weeks after having received the immunizing dose of serum; horse 2 tolerated 50 doses of test toxin two weeks after having received the serum; and the control horse 3 died on the seventh day after having been inoculated with toxin.

EXPERIMENT NO. 1 A

Horse 4 received 1,500 units of antitetanic serum on June 5, 1912. Horse 5 was inoculated with 1,500 units of antitetanic serum on July 5, 1912, and 1,500 units were given to horse 6 on August 5, 1912. Horse 7 was used as control.

On October 5, 1912, each horse received 50 standard test doses of tetanus toxin subcutaneously.

TABLE I A.

No. of animal.	Antitetanic serum units.	Date.	Tetanus toxin test doses.	Date.	Weeks after serum.	Result.	Date.
4	1,500	June 5, 1912	50	Oct. 5. 1912	16	Died	Oct. 9, 1912
5	1,500	do	50	do	12	Died	Oct. 10, 1912
6	1,500	Aug. 5, 1912	50	do	8	Died	Oct. 17, 1912
7	none		50	do		Died	Oct. 9, 1912

As is shown in Table I A, all horses in this series died. Immunity had disappeared eight weeks after the injection of the serum.

EXPERIMENT NO. 2

Of 8 guinea pigs, Nos. 1, 2, 3, 4, 5, 6, 7, and 8, each received three subcutaneous injections of antitetanic serum from horse as follows: February 27, 1911, 10 cubic centimeters; March 4, 10 cubic centimeters; March 11, 10 cubic centimeters.

From May 18, 1911, on every fourth day one guinea pig of the series received subcutaneously 250 units of antitetanic serum as follows: Guinea pig 1, May 18; 2, May 22; 3, May 26; 4, May 30; 5, June 3; 6, June 7; 7, June 11; and 8, June 15.

On June 27, 1911, twelve days after guinea pig 8 received the last injection of antitetanic serum and forty days after guinea pig 1 received the last injection of antitetanic serum, each of

the 8 guinea pigs was inoculated with 0.05 of the test dose of tetanus toxin. Guinea pig 9 served as control; it had not been treated with serum.

TABLE II.

No. of animal.	Anti-tetanic serum. units.	Date.	Tetanus toxin test dose.	Date.	Days after serum.	Result.
1	250	May 18, 1911	0.05	June 27, 1911	40	Died.
2	250	May 22, 1911	0.05	do	36	Died.
3	250	May 26, 1911	0.05	do	32	Lived.
4	250	May 30, 1911	0.05	do	28	Lived.
5	250	June 3, 1911	0.05	do	24	Lived.
6	250	June 7, 1911	0.05	do	20	Lived.
7	250	June 11, 1911	0.05	do	16	Lived.
8	250	June 15, 1911	0.05	do	12	Lived.
9	none		0.05	do		Died.

The results, as shown in Table II, were as follows: Guinea pigs 1, 2, and 9 died while 3, 4, 5, 6, 7, and 8 lived. Guinea pig 3 tolerated 0.05 of the test dose of tetanus toxin on the thirty-second day after having received the antitoxin, while guinea pig 2 did not tolerate the same dose of toxin on the thirty-sixth day after injection of antitoxin.

EXPERIMENT NO. 3

Guinea pigs 10, 11, 12, 13, 14, 15, 16, and 17 each received three subcutaneous injections of normal horse serum as follows: February 27, 1911, 10 cubic centimeters; March 4, 10 cubic centimeters; March 11, 10 cubic centimeters.

Beginning on May 18, 1911, every fourth day one guinea pig of the series received an injection of 250 units of antitetanic serum subcutaneously. Injections were given on the following dates: Guinea pig 10, May 18; 11, May 22; 12, May 26; 13, May 30; 14, June 3; 15, June 7; 16, June 11; 17, June 15, 1911.

On June 27, twelve days after guinea pig 17 had received 250 units of antitetanic serum and forty days after guinea pig 10 was inoculated with antitoxin, each guinea pig in the series was inoculated subcutaneously with 0.05 of the test dose of tetanus toxin. Guinea pig 18 was used as control.

TABLE III.

No. of animal.	Antitetanic serum units.	Date.	Tetanus toxin test dose.	Date.	Days after serum.	Result.
10	250	May 18, 1911	0.05	June 27, 1911	40	Died.
11	250	May 22, 1911	0.05	do	36	Died.
12	250	May 26, 1911	0.05	do	32	Lived.
13	250	May 30, 1911	0.05	do	28	Lived.
14	250	June 3, 1911	0.05	do	24	Lived.
15	250	June 7, 1911	0.05	do	20	Lived.
16	250	June 11, 1911	0.05	do	16	Lived.
17	250	June 15, 1911	0.05	do	12	Lived.
18	none		0.05	do		Died.

The results shown in Table III were as follows: Guinea pigs 10 and 11 and the control 18 died. All others lived. The results obtained in experiment 3 were identical with those obtained in experiment 2.

CONCLUSIONS

The following conclusions seem justified:

1. The subcutaneous injection of 1,500 units of antitetanic serum from horse into horse confers passive immunity of between six and eight weeks' duration.

2. Guinea pigs subjected to repeated inoculations with antitetanic serum from horse do not acquire the power to eliminate it more rapidly; they acquire a tolerance as is shown by the longer period of immunity.

3. After repeated injections of normal horse serum into guinea pigs, passive immunity, following the injection of antitetanic serum from horse, is of longer duration than it is in untreated guinea pigs.

APPENDICITIS [1]

By P. K. GILMAN [2]

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Appendicitis is a disease confined to no particular locality, race, age, or station of life; it is of interest to each and every class; and its pathology and treatment have been developed in our own generation.

As late as 1886 only did R. H. Fitz, a Boston surgeon, clearly point out the cause of the frequent acute, and often fatal, attacks of pain and inflammation in the lower right abdomen. Since that date a long list of surgeons have, by their contributions, succeeded in building up a technique for dealing with the disease in its acute and chronic stages.

Before considering briefly some of the various types of appendicitis with their complications, we wish to make a statement that our experience has borne out. It is a safe rule to consider the possibility of appendicitis in every case of abdominal trouble not clearly due to something else. Therefore, in each case of abdominal disease the physician should endeavor first of all to rule out appendicitis. This should especially be borne in mind by those of us who have not at hand a completely organized hospital with its staff, including a thoroughly equipped clinical laboratory, to assist us in ruling out other conditions and narrowing the field of diagnostic possibilities.

A brief analysis of the last 50 cases of acute appendicitis operated upon in the clinic of the Philippine General Hospital may be of interest at this point. The ages of these patients range from 4 to 55 years, with the greatest number of cases between the ages of 20 and 30.

There were 38 male and 12 female cases. Nineteen of the patients complained of pain beginning in the lower right abdomen; 21 claimed a general abdominal pain, while in the remaining

[1] Read before the Ninth Annual Meeting of the Philippine Islands Medical Association, held in Manila from November 4–7, 1912.

[2] Professor of surgery, College of Medicine and Surgery, University of the Philippines, and chief of the department of surgery, Philippine General Hospital.

number no special mention was made of any marked abdominal discomfort. The initial pain due to obstruction and distension of the lumen of the appendix is often agonizing, although all grades occur. While this pain is present, the disease is confined to the appendix, and this severe pain is usually transient, reaching its height within four hours from the onset and at that time generally localized in the appendix region. Probably 75 per cent of the cases subside at this point—a few in thirty-six hours. If there is a sudden cessation of the pain, this is a danger signal indicating perforation.

We have found the temperature of recently admitted patients to be of comparatively little diagnostic value, as it is well known that the excitement dependent upon change of scene, often irregular transportation, and admission to a hospital will result in a much lower temperature than the patient exhibited before being brought to the institution.

Of the reflex gastrointestinal symptoms, nausea, unaccompanied by actual vomiting, was present in 9 instances, vomiting in 18, constipation in 9, and diarrhœa in but 3 of the series, no disturbance being recorded in the remainder of the cases.

The nausea and vomiting follow the initial pain in the acute cases and are reflex, the nervous mechanism of the appendix being connected with that of the stomach and small intestine. The primary nausea usually subsides fairly promptly.

On examination, tenderness in the region of appendix is practically always present in acute attacks. It is hard to elicit in the very stout and the very nervous. More or less rigidity of the abdominal wall in the lower right quadrant is present, although a careful comparison with the left side is needed in many instances to make this point apparent. Tenderness and rigidity in parts removed from the appendix region are encountered at times and may prove misleading. Four of our cases showed generalized abdominal tenderness, and 1 a marked area sensitive to palpation confined entirely to the left hypogastric region. Eight complained of no special tenderness, the others of soreness higher up than the classical point and often far toward the posterior portion of the body. Exploration of the rectum is often of great importance.

In this clinic where we have come to the point of immediate operation, in every case of acute appendicitis, little stress is now laid on the leucocytic content of the blood in the frank cases. It is in those cases where some doubt exists as to the exact nature of the condition that we depend more upon the result of

the blood examination, where for example a marked leucocytosis may be the most prominent feature of an otherwise masked inflammatory process. The leucocytes are of diagnostic significance when they are increasing.

The highest count met with in these cases of acute appendiceal trouble was 28,000, the operation in this instance revealing an appendix already perforated with localized peritonitis. The lowest count was 6,600 in a case presenting marked rigidity of the lower abdomen with severe pain and tenderness, in which the process, however, was limited to the appendix. One-third of the cases yielded a count below 10,000, all of these being simple acute processes confined to the appendix; another third made up of similar cases gave a count of between 10,000 and 17,000; while those with a higher count included the complicated cases with abscess and peritoneal invasion. Only 4 of this series gave a history of previous dysentery.

The clinical picture presented by the above group of acute cases is too well known to necessitate further elaboration here. It is our purpose to endeavor to emphasize in this communication some of the findings in those cases of more or less obscure nature which manifest themselves in disturbances of varying severity in the digestive apparatus. As our knowledge of the pathology of this probably functionless rudiment is increased, we are forced more and more to regard the appendix as the underlying cause of numerous subacute and chronic disturbances heretofore ascribed to other organs or groups of organs.

It appears a far cry indeed from a case of acute inflammation of the appendix, with its sudden severe pain localized in the right lower quadrant of the abdomen accompanied by nausea, vomiting, diarrhœa, increasing fever, and climbing leucocyte count, to a case of neurasthenia with slight stomach trouble, chronic constipation, and a power of assimilation varying from a little to considerably below normal; and yet we must ascribe the two conditions to the disease of the same organ.

These two apparently widely separated states are linked together by a series of intermediate cases.

To illustrate this latter group of cases, it will be well to give a brief résumé of a few typical cases, illustrating various results of chronic pathological change in the appendix:

CASE I.—American woman, age 40 years, single. For a number of years she had been treated by various physicians for chronic constipation and general nervousness. The patient was well nourished, in spite of troublesome fullness and flatulency of the stomach after taking food,

which was relieved by bringing up considerable amounts of gas between meals. The constipation has grown progressively worse for a period of two years, in spite of various diets, exercises, and increasing doses of purgatives.

The result of a general examination was negative with the exception of a slight increase in the rigidity of the wall of the right lower quadrant of the abdomen over that of the opposite side and a slight tenderness on deep palpation over the cæcal region not due to the pelvic viscera, as determined by bimanual examination. No definite attacks of pain referable to this region of the abdomen were remembered by the patient.

Removal of the appendix was advised, and at operation an appendix nearly obliterated, patent, and of increased diameter for only the distal half-centimeter was found. The proximal portion of the organ was largely represented by a mass of fibrous tissue with evidences of the original layers occurring in but one or two places. There was atrophy of the lining of the distended distal portion. The patient recovered promptly, and within three months of the operation suffered no more from nervousness, indigestion, or constipation.

CASE II.—Physician, age 30, single, complained of recurring jaundice of very slight grade, accompanied by attacks of hyperacidity and constipation. Following one of these attacks, in which there had been a slight febrile reaction unaccompanied by any leucocytosis, the gall bladder had been explored and drained, it being thought that here lay the cause of the trouble. The patient recovered from this attack about as quickly as he had from the previous ones, but, after a period of freedom from jaundice lasting only a little longer than the previous intervals, he again became yellow and had a low fever. During this attack, the intestinal manifestations were more marked than usual, and examination showed on deep palpation a very tender appendix region. An appendix with thickened wall, well surrounded by adhesions and plastered posteriorly to the lower end of the cæcum, was removed through a low incision. During the past five years the patient has been free from all jaundice and digestive disturbances.

CASE III.—American clerk, age 28 years, single. This patient complained of a slight yellow color of the eyeballs, sour stomach, constipation alternating with diarrhœa, and increasing nervousness. The jaundice and the attacks of diarrhœa were to the patient the most annoying symptoms. At no time was there any tenderness elicited by pressure over the region of the gall bladder, although even light palpation over the appendix produced discomfort and a sickening sensation which, although never entirely absent, was most marked during acute exacerbations of the symptoms.

At the time of operation the advisability of exploring the gall bladder was discussed, and, as it was found possible completely to empty this organ with the finger introduced through a McBurney incision, the operation included merely the removal of the appendix, which was chronically inflamed, adherent, with signs of acute engorgement. It is now over three years since the operation, and the patient has had no further jaundice nor other manifestation of a gastrointestinal disturbance.

CASE IV.—American woman, aged 42, married, has had several children, and has lived in tropical countries for over twelve years. For the past three years or more the patient has lost weight slowly but steadily, and has had numerous attacks of jaundice of a mild grade with no special

pain referable to the gall-bladder region. There has been a gradually increasing discomfort and sensation of weight in the lower right side of the abdomen, which became actual pain, accompanied by soreness, when the yellow color of the eyes and skin was most marked. During the last attack, a month ago, the patient suffered some pain below the right costal margin, was definitely jaundiced, and the appendix region was very tender with increased rigidity of the superimposed walls.

At the operation the gall bladder was found rather thickened and did not empty readily. For this reason, following the removal of an adherent chronically thickened appendix, the gall bladder was opened, a tarry bile evacuated, and the bladder drained. No evidence of stone was found in this case. Already the jaundice has completely cleared, the digestion has been restored to practically normal, and a gain of several pounds has been made.

The above are but a few of a considerable series of cases showing concurrent disease of the appendix and gall bladder. Given these conditions, a simple drainage of the gall bladder without the removal of the appendix will not insure a freedom from recurring trouble with the biliary apparatus.

In looking over our records of gall-bladder disease where it was possible to follow the patients for any length of time after their operations of drainage for a simple cholecystitis, we find in some instances a fairly prompt recurrence of the jaundice and so-called "stomach trouble." Might not these cases have had enough symptoms above the umbilicus to cause the examining physician to overlook the presence of trouble in the appendix?

Another group of cases of appendicitis with which we have had a rather fortunate experience is the group made up of cases in which the mildness of the symptoms has been out of all proportion to the condition found at operation.

CASE I.—American, aged 32, married, clerk. Entered the hospital complaining of stomach trouble. The patient was very stout, and examination was difficult, but a slight tenderness was elicited over the right iliac fossa in which region a slight general abdominal pain was localized. The leucocyte count upon admission was 8,000. There was practically no fever, and the patient's wife refused her consent to an operation for appendicitis. Twenty-four hours later the pain had increased somewhat, although it was not very severe, the temperature had risen to 38°.2 C., and the leucocytes were 15,000. Operation was again advised and consent given rather reluctantly, as the patient did not appear very uncomfortable. At operation, performed about thirty hours after the first complaint, the appendix was found gangrenous and free in the abdominal cavity, together with a general collection of bowel contents and pus with practically no attempt at localization on the part of the peritoneum and viscera. The cæcum was found greatly thickened and in places puckered and pigmented as though from the old dysentery from which this patient had suffered two years previous to the operation. The patient fortunately recovered from the peritonitis, and is to-day well.

CASE II.—American, aged 40, clerk, walked into the hospital, complained of abdominal discomfort and, as he had had several attacks of amœbic dysentery, was admitted to the medical service. The patient continued up and about the ward during the first day of his stay in the hospital; however, as the abdominal discomfort continued, the surgeon was asked to see the case, the resident physician in medicine having followed the course of events in Case No. I a few days before the present case was admitted to the ward.

This case presented a flat, easily examined abdomen, which showed nothing of interest save a thickened large bowel with general slight tenderness a little more marked below the level of the umbilicus, with practically no increased rigidity of the abdominal wall. The leucocytes numbered between 13,000 and 14,000.

Operation was advised, and, with the other case with a history of recurrent dysentery in mind, was performed at once, the patient walking into the operating room unassisted. The appendix was found perforated near the base. The entire structure, as well as the walls of the entire large bowel, was greatly thickened and leathery. The peritoneum contained a considerable amount of bowel content and fibrin, fairly well localized to the lower right quadrant. The lack of pain and the extremely slight reaction on the part of the patient to the condition found were remarkable in this case, even more so than in the previous one. From these two cases and others of a similar type it would seem that the resulting chronic changes in the bowel and peritoneum following recurring attacks of amœbic dysentery extending over a long period have exerted a definite influence. Neither of the above cases has had a recurrence of dysentery since the removal of the appendix.

We have then a group of cases of appendicitis occurring in persons, especially Europeans, who have had a previous dysentery extending over some time, in which cases the pathological processes may have progressed to a point out of all proportion to the manifestations of the disease exhibited clinically, and it is in these cases that we must exercise great care lest we make the mistake of not emphasizing sufficiently the necessity for immediate operative interference.

We have purposely laid less emphasis upon acute appendicitis, as it is not only more readily diagnosed than the various chronic forms, but its differentiation from other conditions—such as a perforated ulcer of the stomach or duodenum—is, so far as treatment is concerned, not so essential since both conditions demand immediate surgical intervention. On the other hand, it is the more or less obscure cases dependent upon a slowly progressing chronic change in the appendix, often without definite indications pointing to this organ as the underlying cause, to which we wish particularly to draw attention. If we will recall that the variety of the manifestations of these chronic changes may be innumerable and consider the possibility of appendicitis

in every case of abdominal trouble not clearly due to something else, we shall be in a position to relieve a large number of patients who heretofore have drifted from one physician to another. Too often these patients tell of various diagnoses by different physicians and of long courses of treatment for disorders attributed at different times to various portions of the alimentary canal.

Appendicitis as met with in the Philippines presents, among both the Filipinos and Europeans who have resided here for long periods, certain differences from the cases usually met with in the United States. This disease is not always a simple matter to diagnose nor, if a diagnosis has been made, is the condition of the appendix and neighboring peritoneum always an easy question to determine. In many cases pathological changes occur which are out of all proportion to the clinical manifestations.

THE PHILIPPINE ISLANDS MEDICAL ASSOCIATION

MINUTES OF THE NINTH ANNUAL MEETING

The ninth annual meeting of the Philippine Islands Medical Association was held in the histological laboratory of the College of Medicine and Surgery, November 4 to 7, 1912, inclusive.

FIRST SESSION, NOVEMBER 4, 9 A. M.

The first session was called to order by President Newberne, who made a few remarks of welcome and introduced the Acting Governor-General, who presided at the opening session. The Acting Governor-General made some interesting remarks relative to medical men, sanitation in the Philippines, medical education, and the Philippine Islands Medical Association. The Acting Governor-General turned the chair over to the Honorable the Secretary of the Interior, who presided during the address of President Newberne on "Basic Principles of Psychotherapy and the Identity of all Mental Healing Systems."

The following scientific program was next presented and carried out in the order indicated:

Two Cases of Primary Purpura, by José Albert and María Paz Mendoza.

A Case of Microcephalus with Symptoms of Tetanus, by José Albert and María Paz Mendoza.

A Study of 100 Cases of Lobar Pneumonia in the Tropics, by C. R. Stanley. (Read by title.)

Cutaneous Anthrax, with Report of a Case, by E. C. White.

A Case of True Bilharzial Disease in Porto Rico, by U. R. Webb.

Korsakow's Psychosis, with Report of a Case, by Heber Butts.

Congenital Varicosities of the Venæ Epigastricæ Superiores, Paraumbilicalæ, Thoracoepigastricæ, and Mammariæ, by A. G. Sison.

Elephantiasis Congenitalis Glabra, with Report of a Case, by Honoria Acosta Sison.

Bone Lesions in Smallpox, by W. E. Musgrave and A. G. Sison. (Discussion by Major Ashburn and Dr. Heiser.)

Glandular Fever, by Almon P. Goff.

Number present, 76.

Meeting adjourned at 12.30 p. m.

SECOND SESSION, NOVEMBER 5, 9 A. M.

Status Thymico-Lymphaticus in Filipinos, by B. C. Crowell. (Discussion by Major Ashburn and Dr. Crowell.)

Sarcoma of Intestine, Pathological Anatomy, with Report of Cases, by R. W. Hammack.

A Tumor of the Hypophysis Cerebri, by José Hilario.

Presentation of pathological specimens, department of pathology and bacteriology, College of Medicine and Surgery, University of the Philippines.

The Rôle of the Individual Proteins in Nutrition, by R. B. Gibson.

Polyneuritis Gallinarum—

(*a*) The Influence of Various Foodstuffs on its Development, by Edward B. Vedder.

(*b*) Early Changes in the Peripheral Nerves, by Elbert Clark.

Infant Mortality in Manila—

(*a*) General Considerations, by W. E. Musgrave.

(The papers by R. B. Gibson, Edward B. Vedder, Elbert Clark, and W. E. Musgrave, all being related from a nutritional standpoint, were discussed together by Dr. Heiser, Dr. Vedder, Dr. Shaklee, Dr. Gibson, Mr. Clark, Mr. Williams, and Dr. Yemans.)

Experimental Acclimatization of the Philippine Monkey to a Tropical Sun, by A. O. Shaklee.

Sunlight, by Paul C. Freer and Harry D. Gibbs.

(The paper of Dr. Shaklee and that of Dr. Freer and Mr. Gibbs were discussed by Mr. Clark and Major Ashburn.)

Number present, 69.

Meeting adjourned at 12.45 p. m.

THIRD SESSION, NOVEMBER 6, 7.30 A. M.

The surgical clinic with operations at the Philippine General Hospital was given at 7.30 a. m. by Drs. P. K. Gilman and Hans Schiffbauer.

The session convened for the following program at 10 a. m.

The Outbreak of Plague in Manila in 1912, by Victor G. Heiser.

Bacteriological Observations made during the Outbreak of Plague in Manila in 1912, by Otto Schöbl.

The Outbreak of Plague in Iloilo in 1912, by Carroll Fox.

(The above papers were discussed by Drs. Jackson, Ashburn, Crowell, Gibson, Butler, Yemans, Newberne, Heiser, Gomez, Fox, and Schöbl.)

Surgical Treatment of Gonorrhœal Orchitis and Epididymitis, by B. L. Burdette.

Races of Dysentery Bacilli obtained by the Selection of Single Cells, by M. A. Barber. (Read by title.)

Number present, 85.

Meeting adjourned at noon.

FOURTH SESSION, NOVEMBER 6, 2 P. M.

Intra-orbital Tumors and Their Operative Consideration, by Rheinhard Rembe.

Notes on Some Recent Surgical Cases at the Naval Hospital, Cañacao, by N. J. Blackwood. (Discussion by Drs. Burdette and Schiffbauer.)

A Review of the Literature on Cultivation of Fresh Tissues in Various Media, by R. M. Lhamon. (Discussion by Mr. Clark.)

Diagnosis of Appendicitis, by P. K. Gilman.

Treatment of Acute Appendicitis, by Hans Schiffbauer. (Discussion by Drs. Burdette, Blackwood, Lhamon, Newberne, Schiffbauer, and Gilman.)

A Preliminary Report of the First Five Cases of Cæsarian Section in the Treatment of Placenta Prævia Performed in the Philippine Islands, by Fernando Calderon.

Number present, 38.

Meeting adjourned at 4.30 p. m.

FIFTH SESSION, NOVEMBER 7, 9 A. M.

Clinic in department of diseases of the eye, ear, nose, and throat, Philippine General Hospital, by Dr. Rembe and assistants.

Some Carbohydrate Reactions of the Dysentery Bacillus, by C. S. Butler. (Discussion by Dr. Gibson.)

Isolation of *Diplococcus intracellularis meningitidis* Weichselbaum from a Case of Cerebrospinal Meningitis Occurring in a Native of the Philippine Islands, by David G. Willetts and Otto Schöbl. (Discussion by Drs. Heiser and Gentry.)

The Duration of Passive Immunity against Tetanus Toxin, by E. H. Ruediger.

Quantitative Determination of the Balantidicidal Action of Drugs and Chemicals as a Basis for the Treatment of Balantidial

Dysentery, by E. L. Walker. (Discussion by Drs. C. S. Butler and E. B. Vedder.)

Salvarsan in Malaria, by R. H. Goldthwaite.

Experiences in Anæsthesia at the Philippine General Hospital, by E. J. Ochsner. (Discussion by Drs. Blackwood and Heiser.)

Artificial Ears and Noses, by Louis Ottofy.

The Military Importance of Deviations of the Nasal Septum, by T. C. Lyster. (Read by title.)

Sanitation in Small Towns in the Philippine Islands, by Frank Baker. (Read by title.)

Ancient Medical Customs among the Japanese, by Dr. Yegawa. (Read by title.)

Number present, 41.

AFTERNOON

Medical clinics at the Philippine General Hospital (at 2 p. m.), by W. E. Musgrave and José Albert.

BUSINESS MEETINGS

FIRST BUSINESS SESSION, NOVEMBER 4, 4 P. M.

At the first meeting of the House of Delegates, the president called attention to a proposed amendment to the constitution which was read before the association at the eighth annual meeting, and which provided that the council consist solely of ex-presidents of the Association.

After discussion, it was decided to leave the consideration of this to a committee who was instructed to report at the business meeting. The president appointed Major Ashburn, Dr. Heiser, and Surgeon Butler a committee on nominations. This committee was also instructed to consider and report upon the proposed amendment.

SECOND BUSINESS SESSION, NOVEMBER 7, 12.30 P. M.

Roll call and reading of minutes were passed over.

The secretary made a verbal report. All of the expenses of the meeting not being ascertainable at this time, he promised a written report to be submitted to the council.

There being no unfinished business, motions under the head of "new business" were next considered.

Dr. Heiser suggested and proposed that, in view of the recent advances in the work concerning the etiology of beriberi, and in view of the confirmation of the former theory concerning the close interrelation of polished rice diet and beriberi, the Philippine Islands Medical Association propose, through the proper

channels, to the Philippine Legislature now in session, the following resolution:

Resolved, That in the opinion of this Association, sufficient evidence has been produced in support of the view that beriberi is associated with the continuous consumption of decorticated rice as a staple article of diet; that this Association strongly recommends to the Philippine Legislature the passage of suitable legislation which will have for its object the bringing about of the general use of unpolished rice among those who use it as a staple article of diet.

The proposed amendment to the constitution that all ex-presidents be considered members of the council of the Philippine Islands Medical Association, and that the council consist solely of ex-presidents was brought before the house by the president. This was proposed at the eighth annual meeting.

After discussion, the amendment was rejected.

REPORT OF THE COMMITTEE OF THE HOUSE OF DELEGATES

The committee of the House of Delegates, appointed by the president at the first meeting of the House of Delegates on Monday the 4th, submitted its report.

Dr. R. P. Strong was recommended by the committee as a delegate to the next annual meeting of the American Medical Association to be held in Minneapolis, June 15, 1913.

The committee further recommended that the incoming president appoint an alternate, it being impossible to determine at this time what member of the Association will be in America at the time of the meeting of the American Medical Association.

The secretary was instructed to cast a vote for Dr. Strong, and this part of the report of the committee was adopted.

The same committee recommended that the same method of procedure be employed in the selection of a delegate to the next annual meeting of the Far Eastern Association of Tropical Medicine to be held in Saigon. After motion, the suggestion was adopted.

The same committee submitted the following ballot for officers for the ensuing year:

President: Surgeon N. J. Blackwood, U. S. Navy.

Vice-presidents: Dr. N. M. Saleeby and Dr. A. G. Sison.

Councillor for five years: Dr. R. E. L. Newberne.

Upon motion, which was seconded and passed, the secretary was instructed to cast the ballot for this ticket.

On the suggestion of the president, it was unanimously moved that a vote of thanks be extended by the Philippine Islands

Medical Association to Dr. Woodbury, of the Philippine General Hospital, for furnishing plants for decoration; to Dr. Alvin J. Cox, Acting Director of the Bureau of Science, for the erection, free of charge, of a platform; and to Mrs. S. E. Waddington, of the University of the Philippines, for decorating the platform and arranging bouquets for the ninth annual meeting of this Association.

On motion of Major Ashburn, which was amended by Dr. Heiser and the secretary, a vote of appreciation was extended by the association to the president for his keen interest in the ninth annual meeting; to the Honorable Dean C. Worcester for furnishing entertainment for the social evening, and to such other officers and committees which took an active interest in making the ninth annual meeting a success.

President Newberne expressed his appreciation of the work of the other officers and of the committees, and for the good attendance and interest which was manifested in the various sessions.

The secretary was instructed to inform each of the above persons of this action by the Association.

There being no further business, the ninth annual session of the Philippine Islands Medical Association adjourned.

After the annual meeting had adjourned, the members and their guests gathered at the roof garden of the Manila Hotel and were favored by a most interesting illustrated lecture on Wild Tribes in northern Luzon by the Honorable the Secretary of the Interior, Dean C. Worcester.

Secretary Worcester showed some interesting motion pictures, and told many interesting personal details of the plan of civilization and his experiences in northern Luzon.

After the lecture, a buffet lunch was served, and the members enjoyed a pleasant social evening.

The committee on exhibits arranged the exhibits in the physiological laboratory, and the pathological museum was open to inspection. Exhibits were shown by the department of physiology and of pathology and bacteriology of the College of Medicine and Surgery, by Dr. Louis Ottofy and by Dr. Mariano V. del Rosario. Exhibits were also arranged by Parke, Davis & Co., the German Dispensary, Philippine Education Publishing Company, Pacific Commercial Company, Nestle Anglo-Swiss Milk Company, and by the PHILIPPINE JOURNAL of SCIENCE.

ELBERT CLARK,
Acting Secretary, Philippine Islands Medical Association.